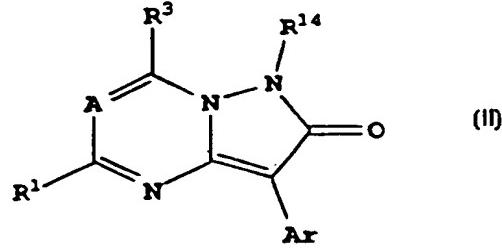
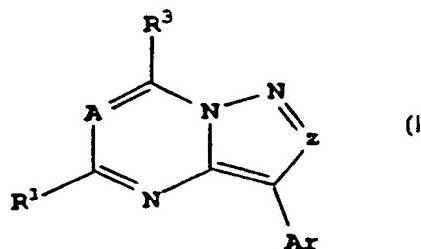




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 487/04, A61K 31/495 // (C07D 487/04, 251:00, 231:00) (C07D 487/04, 239:00, 231:00)		A1	(11) International Publication Number: WO 99/38868 (43) International Publication Date: 5 August 1999 (05.08.99)
(21) International Application Number: PCT/US99/01824		(81) Designated States: AU, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 28 January 1999 (28.01.99)		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(30) Priority Data: 09/015,002 28 January 1998 (28.01.98) US 09/014,734 28 January 1998 (28.01.98) US 09/015,001 28 January 1998 (28.01.98) US			
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(54) Title: AZOLO TRIAZINES AND PYRIMIDINES



(57) Abstract

Corticotropin releasing factor (CRF) antagonists of formula (I) or (II) and their use in treating anxiety, depression, and other psychiatric, neurological disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress.

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TITLE

AZOLO TRIAZINES AND PYRIMIDINES

5

FIELD OF THE INVENTION

This invention relates a treatment of psychiatric disorders and neurological diseases including major depression, anxiety-related 10 disorders, post-traumatic stress disorder, supranuclear palsy and feeding disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and 15 stress, by administration of certain [1,5-a]-pyrazolo-1,3,5-triazines, [1,5-a]-1,2,3-triazolo-1,3,5-triazines, [1,5-a]-pyrazolo-pyrimidines and [1,5-a]-1,2,3-triazolo-pyrimidines.

20

BACKGROUND OF THE INVENTION

Corticotropin releasing factor (herein referred to as CRF), a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC) -derived peptide secretion from the anterior 25 pituitary gland [J. Rivier et al., *Proc. Nat. Acad. Sci. (USA)* 80:4851 (1983); W. Vale et al., *Science* 213:1394 (1981)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the 30 hormone has a broad extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain

[W. Vale et al., *Rec. Prog. Horm. Res.* 39:245 (1983); G.F. Koob, *Persp. Behav. Med.* 2:39 (1985); E.E. De Souza et al., *J. Neurosci.* 5:3189 (1985)]. There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological, psychological, and immunological stressors [J.E. Blalock, *Physiological Reviews* 69:1 (1989); J.E. Morley, *Life Sci.* 41:527 (1987)].

10 Clinical data provide evidence that CRF has a role in psychiatric disorders and neurological diseases including depression, anxiety-related disorders and feeding disorders. A role for CRF has also been postulated in the etiology and
15 pathophysiology of Alzheimer's disease, Parkinson's disease, Huntington's disease, progressive supranuclear palsy and amyotrophic lateral sclerosis as they relate to the dysfunction of CRF neurons in the central nervous system [for review see E.B. De
20 Souza, *Hosp. Practice* 23:59 (1988)].

In affective disorder, or major depression, the concentration of CRF is significantly increased in the cerebral spinal fluid (CSF) of drug-free individuals [C.B. Nemeroff et al., *Science* 226:1342 (1984); C.M. Banki et al., *Am. J. Psychiatry* 144:873 (1987); R.D. France et al., *Biol. Psychiatry* 28:86 (1988); M. Arato et al., *Biol Psychiatry* 25:355 (1989)]. Furthermore, the density of CRF receptors is significantly decreased in the frontal cortex of
30 suicide victims, consistent with a hypersecretion of CRF [C.B. Nemeroff et al., *Arch. Gen. Psychiatry* 45:577 (1988)]. In addition, there is a blunted

adrenocorticotropin (ACTH) response to CRF (i.v. administered) observed in depressed patients [P.W. Gold et al., *Am J. Psychiatry* 141:619 (1984); F. Holsboer et al., *Psychoneuroendocrinology* 9:147 (1984); P.W. Gold et al., *New Eng. J. Med.* 314:1129 (1986)]. Preclinical studies in rats and non-human primates provide additional support for the hypothesis that hypersecretion of CRF may be involved in the symptoms seen in human depression [R.M. Sapolsky, *Arch. Gen. Psychiatry* 46:1047 (1989)]. There is preliminary evidence that tricyclic antidepressants can alter CRF levels and thus modulate the numbers of CRF receptors in brain [Grigoriadis et al., *Neuropsychopharmacology* 2:53 (1989)].

There has also been a role postulated for CRF in the etiology of anxiety-related disorders. CRF produces anxiogenic effects in animals and interactions between benzodiazepine / non-benzodiazepine anxiolytics and CRF have been demonstrated in a variety of behavioral anxiety models [D.R. Britton et al., *Life Sci.* 31:363 (1982); C.W. Berridge and A.J. Dunn *Regul. Peptides* 16:83 (1986)]. Preliminary studies using the putative CRF receptor antagonist a-helical ovine CRF (9-41) in a variety of behavioral paradigms demonstrate that the antagonist produces "anxiolytic-like" effects that are qualitatively similar to the benzodiazepines [C.W. Berridge and A.J. Dunn *Horm. Behav.* 21:393 (1987), *Brain Research Reviews* 15:71 (1990)]. Neurochemical, endocrine and receptor binding studies have all demonstrated interactions between CRF and benzodiazepine

anxiolytics providing further evidence for the involvement of CRF in these disorders.

Chlordiazepoxide attenuates the "anxiogenic" effects of CRF in both the conflict test [K.T. Britton et al., *Psychopharmacology* 86:170 (1985); K.T. Britton et al., *Psychopharmacology* 94:306 (1988)] and in the acoustic startle test [N.R. Swerdlow et al., *Psychopharmacology* 88:147 (1986)] in rats. The benzodiazepine receptor antagonist (Ro15-1788), which was without behavioral activity alone in the operant conflict test, reversed the effects of CRF in a dose-dependent manner while the benzodiazepine inverse agonist (FG7142) enhanced the actions of CRF [K.T. Britton et al., *Psychopharmacology* 94:306 (1988)].

The mechanisms and sites of action through which the standard anxiolytics and antidepressants produce their therapeutic effects remain to be elucidated. It has been hypothesized however, that they are involved in the suppression of the CRF hypersecretion that is observed in these disorders. Of particular interest is that preliminary studies examining the effects of a CRF receptor antagonist (α -helical CRF9-41) in a variety of behavioral paradigms have demonstrated that the CRF antagonist produces "anxiolytic-like" effects qualitatively similar to the benzodiazepines [for review see G.F. Koob and K.T. Britton, In: *Corticotropin-Releasing Factor: Basic and Clinical Studies of a Neuropeptide*, E.B. De Souza and C.B. Nemeroff eds., CRC Press p221 (1990)].

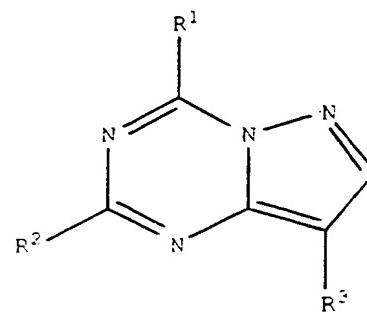
Several publications describe corticotropin releasing factor antagonist compounds

DM

and their use to treat psychiatric disorders and neurological diseases. Examples of such publications include DuPont Merck PCT application US94/11050, Pfizer WO 95/33750, Pfizer WO 95/34563, 5 Pfizer WO 95/33727 and Pfizer EP 0778 277 A1.

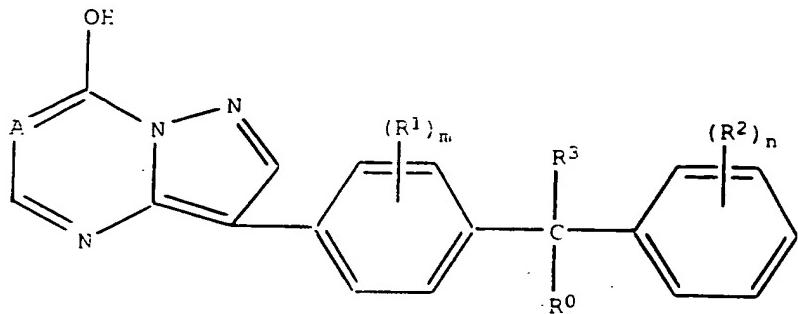
Insofar as is known, [1,5-a]-pyrazolo-1,3,5-triazines, [1,5-a]-1,2,3-triazolo-1,3,5-triazines, [1,5-a]-pyrazolo-pyrimidines and [1,5-a]-1,2,3-triazolo-pyrimidines, have not been previously 10 reported as corticotropin releasing factor antagonist compounds useful in the treatment of psychiatric disorders and neurological diseases. However, there have been publications which teach some of these compounds for other uses.

15 For instance, EP 0 269 859 (Ostuka, 1988) discloses pyrazolotriazine compounds of the formula



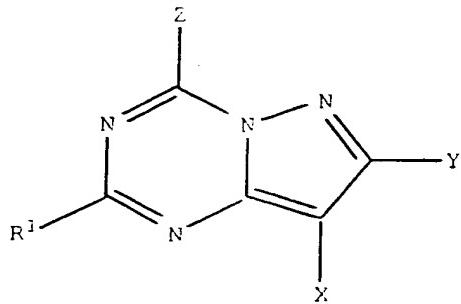
20 where R¹ is OH or alkanoyl, R² is H, OH, or SH, and R³ is an unsaturated heterocyclic group, naphthyl or substituted phenyl, and states that the compounds have xanthine oxidase inhibitory activity and are useful for treatment of gout.

25 EP 0 594 149 (Ostuka, 1994) discloses pyrazolotriazine and pyrazolopyrimidine compounds of the formula



where A is CH or N, R⁰ and R³ are H or alkyl, and R¹ and R² are H, alkyl, alkoxy, alkylthio, nitro, etc., and states that the compounds inhibit androgen and are useful in treatment of benign prostatic hypertrophy and prostatic carcinoma.

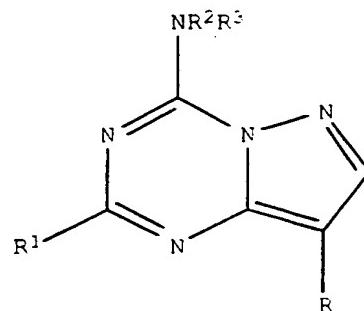
10 US 3,910,907 (ICI, 1975) discloses pyrazolotriazines of the formula:



15 where R1 is CH₃, C₂H₅ or C₆H₅, X is H, C₆H₅, m-CH₃C₆H₄, CN, COOEt, Cl, I or Br, Y is H, C₆H₅, o-CH₃C₆H₄, or p-CH₃C₆H₄, and Z is OH, H, CH₃, C₂H₅, C₆H₅, n-C₃H₇, i-C₃H₇, SH, SCH₃, NH₂, or N(C₂H₅)₂, and states that the compounds are c-AMP phosphodiesterase inhibitors useful as bronchodilators.

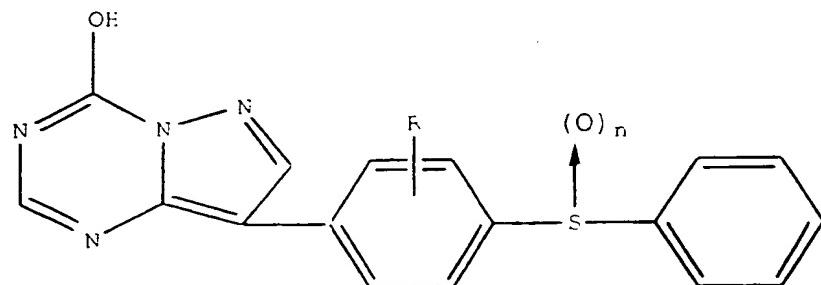
20 US 3,995,039 discloses pyrazolotriazines of

the formula:



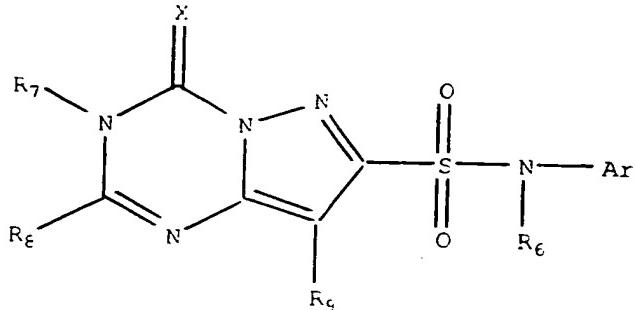
5 where R¹ is H or alkyl, R² is H or alkyl, R³ is H, alkyl, alkanoyl, carbamoyl, or lower alkylcarbamoyl, and R is pyridyl, pyrimidinyl, or pyrazinyl, and states that the compounds are useful as bronchodilators.

10 US 5,137,887 discloses pyrazolotriazines of the formula



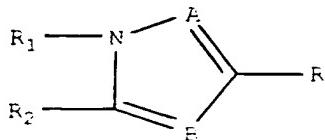
15 where R is lower alkoxy, and teaches that the compounds are xanthine oxidase inhibitors and are useful for treatment of gout.

20 US 4,892,576 discloses pyrazolotriazines of the formula

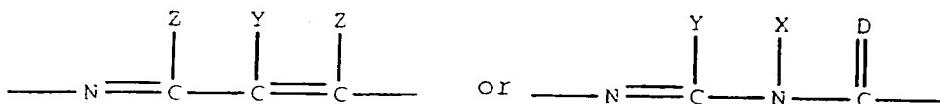


where X is O or S, Ar is a phenyl, naphthyl, pyridyl or thienyl group, R₆-R₈ are H, alkyl, etc., and R₉ is H, alkyl, phenyl, etc. The patent states that the compounds are useful as herbicides and plant growth regulators.

US 5,484,760 and WO 92/10098 discloses herbicidal compositions containing, among other things, a herbicidal compound of the formula



where A can be N, B can be CR₃, R₃ can be phenyl or substituted phenyl, etc., R is -N(R₄)SO₂R₅ or -SO₂N(R₆)R₇ and R₁ and R₂ can be taken together to form

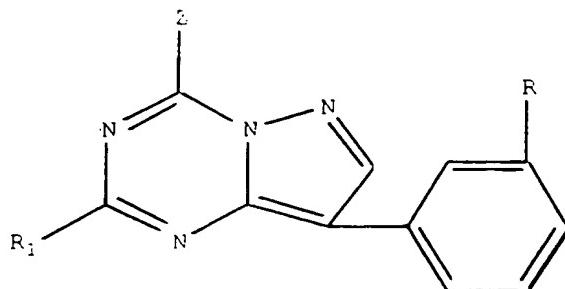


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where X, Y and Z are H, alkyl, acyl, etc. and D is O or S.

US 3,910,907 and Senga et al., J. Med. Chem.,

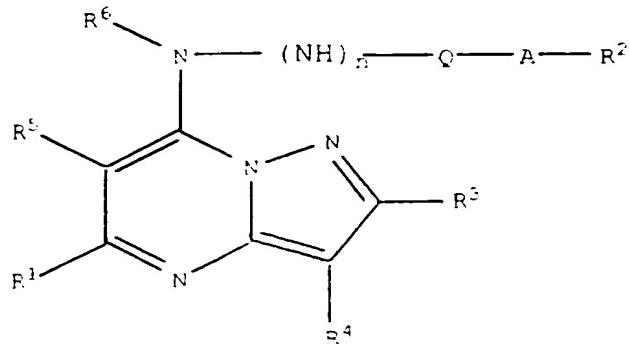
1982, 25, 243-249, disclose triazolotriazines cAMP phosphodiesterase inhibitors of the formula



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where Z is H, OH, CH₃, C₂H₅, C₆H₅, n-C₃H₇, iso-C₃H₇, SH, SCH₃, NH(n-C₄H₉), or N(C₂H₅)₂, R is H or CH₃, and R₁ is CH₃ or C₂H₅. The reference lists eight therapeutic areas where inhibitors of cAMP phosphodiesterase could have utility: asthma, diabetes mellitus, female fertility control, male infertility, psoriasis, thrombosis, anxiety, and hypertension.

15 WO95/35298 (Otsuka, 1995) discloses pyrazolopyrimidines and states that they are useful as analgesics. The compounds are represented by the formula

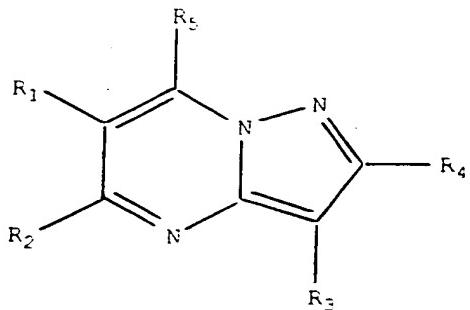


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where Q is carbonyl or sulfonyl, n is 0 or 1, A is a

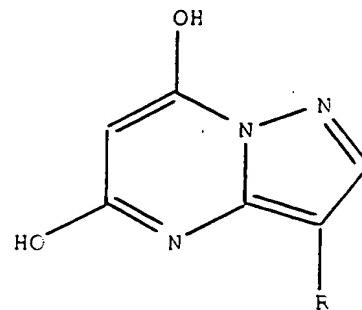
single bond, alkylene or alkenylene, R¹ is H, alkyl, etc., R² is naphthyl, cycloalkyl, heteroaryl, substituted phenyl or phenoxy, R³ is H, alkyl or phenyl, R⁴ is H, alkyl, alkoxycarbonyl, phenylalkyl, 5 optionally phenylthio-substituted phenyl, or halogen, R⁵ and R⁶ are H or alkyl.

EP 0 591 528 (Otsuka, 1991) discloses anti-inflammation use of pyrazolopyrimidines represented by
10 the formula



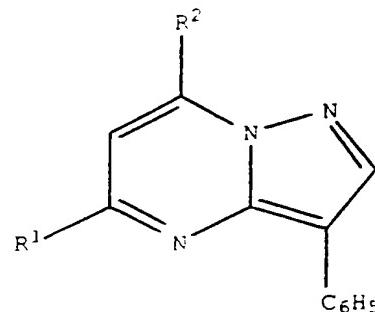
where R₁, R₂, R₃ and R₄ are H, carboxyl,
15 alkoxycarbonyl, optionally substituted alkyl, cycloalkyl, or phenyl, R₅ is SR₆ or NR₇R₈, R₆ is pyridyl or optionally substituted phenyl, and R₇ and R₈ are H or optionally substituted phenyl.

20 Springer et al, J. Med. Chem., 1976, vol. 19, no. 2, 291-296 and Springer U.S. patents 4021,556 and 3,920,652 disclose pyrazolopyrimidines of the formula



where R can be phenyl, substituted phenyl or pyridyl,
and their use to treat gout, based on their ability to
5 inhibit xanthine oxidase.

Joshi et al., J. Prakt. Chemie, 321, 2, 1979,
341-344, discloses compounds of the formula

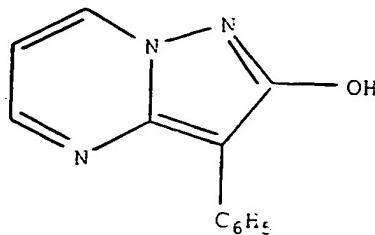


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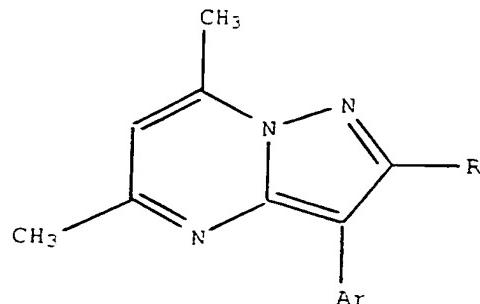
where R¹ is CF₃, C₂F₅, or C₆H₄F, and R² is CH₃, C₂H₅,
CF₃, or C₆H₄F.

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Maquestiau et al., Bull. Soc. Belg., vol.101,
no. 2, 1992, pages 131-136 discloses a pyrazolo[1,5-
a]pyrimidine of the formula



Ibrahim et al., Arch. Pharm. (weinheim) 320, 487-491 (1987) discloses pyrazolo[1,5-a]pyrimidines of
5 the formula



where R is NH₂ or OH and Ar is 4-phenyl-3-cyano-2-
10 aminopyrid-2-yl.

Other references which disclose
azolopyrimidines included EP 0 511 528 (Otsuka, 1992),
US 4,997,940 (Dow, 1991), EP 0 374 448 (Nissan, 1990),
15 US 4,621,556 (ICN, 1997), EP 0 531 901 (Fujisawa, 1993),
US 4,567,263 (BASF, 1986), EP 0 662 477 (Isagro, 1995),
DE 4 243 279 (Bayer, 1994), US 5,397,774 (Upjohn,
1995), EP 0 521 622 (Upjohn, 1993), WO 94/109017
(Upjohn, 1994), J. Med. Chem., 24, 610-613 (1981), and
20 J. Het. Chem., 22, 601 (1985).

SUMMARY OF THE INVENTION

In accordance with one aspect, the present

invention provides novel compounds, pharmaceutical compositions and methods which may be used in the treatment of affective disorder, anxiety, depression, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal disease, anorexia nervosa or other feeding disorder, drug or alcohol withdrawal symptoms, drug addiction, inflammatory disorder, fertility problems,

5 disorders, the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or a disorder selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis,

10 15 pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic, phobias, obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress-induced headache; cancer, human immunodeficiency virus (HIV) infections;

20 25 neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases such as ulcers, irritable bowel syndrome, Crohn's disease, spastic colon, diarrhea, and post operative ileus and colonic hypersensitivity associated by psychopathological disturbances or stress; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of

30 35

inappropriate antidiarrhetic hormone (ADH); obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage (e.g., cerebral ischemia such as cerebral hippocampal ischemia); excitotoxic neuronal damage; epilepsy; cardiovascular and heart related disorders including hypertension, tachycardia and congestive heart failure; stroke; immune dysfunctions including stress induced immune dysfunctions (e.g., stress induced fevers, porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, and dysfunctions induced by confinement in chickens, sheering stress in sheep or human-animal interaction related stress in dogs); muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; chemical dependencies and addictions (e.g., dependencies on alcohol, cocaine, heroin, benzodiazepines, or other drugs); drug and alcohol withdrawal symptoms; osteoporosis; psychosocial dwarfism and hypoglycemia in a mammal.

The present invention provides novel compounds which bind to corticotropin releasing factor receptors, thereby altering the anxiogenic effects of CRF secretion. The compounds of the present invention are useful for the treatment of psychiatric disorders and neurological diseases, anxiety-related disorders, post-traumatic stress disorder, supranuclear palsy and feeding disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress in a mammal.

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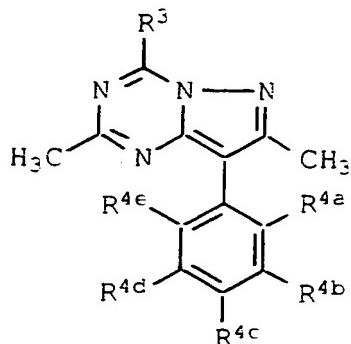
According to another aspect, the present invention provides novel compounds described below which are useful as antagonists of the corticotropin releasing factor. The compounds of the present invention exhibit activity as corticotropin releasing factor antagonists and appear to suppress CRF hypersecretion. The present invention also includes pharmaceutical compositions containing such compounds of Formulae (1) and (2), and methods of using such compounds for the suppression of CRF hypersecretion, and/or for the treatment of anxiogenic disorders.

According to yet another aspect of the invention, the compounds provided by this invention (and especially labelled compounds of this invention) are also useful as standards and reagents in determining the ability of a potential pharmaceutical to bind to the CRF receptor.

20

DETAILED DESCRIPTION OF INVENTION

[1] The present invention provides compounds of
25 Formula (50)



FORMULA (50)

- 5 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, selected from the group:
- 10 a compound of Formula (50) wherein R³ is -NHCH(CH₂CH₂OMe)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 30 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,

- R^{4c} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 20 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 30 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,

- R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,

- R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is

- N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
N(Et)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and
R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and
R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and
R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
H;
- 30 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a}
is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
H;
- 35 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is Me and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 5 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

- a compound of Formula (50) wherein R³ is
N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;
5
- a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
Me;
- 40 a compound of Formula (50) wherein R³ is NHCH(cPr)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is Me;

- a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- 5
- a compound of Formula (50) wherein R³ is
 N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is OMe;
- 10
- a compound of Formula (50) wherein R³ is
 N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is OMe;
- 15
- a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40
- a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,

R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

5 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

10 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

20 15 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

25 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

30 25 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

40 35 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
40 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H.

and R^{4e} is OMe;

5 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

10 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

20 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

25 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

45 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,

- R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is
N(Et)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H.
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 45 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F

and R^{4e} is H;

- 5 a compound of Formula (50) wherein R^3 is
 $N(Me)CH_2CH=CH_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is
 $N(Et)CH_2CH=CH_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 20 a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 25 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 30 a compound of Formula (50) wherein R^3 is $N(Me)Et$, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is
H;
- 35 a compound of Formula (50) wherein R^3 is
 $N(Me)propargyl$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is F and R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is
 $NH(CH(CH_3)CH(CH_3)CH_3$, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)$ -

- CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is F, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H.
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R³ is

- N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is
 $NH(CH_2CH_3)CH(CH_3)CH_3$, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)-$
 $CH_2CH=CH_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is
 $N(CH_2CH_2OMe)Me$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R^3 is
 $N(CH_2CH_2OMe)Et$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)-$
 CH_2cPr , R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R^3 is
 $NHCH(CH_3)CH_2CH_3$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)_2$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is

H;

5 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

20 15 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

30 25 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

40 35 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

45 40 a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- 5
- a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10
- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15
- a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40
- a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH₂CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R³ is NHCH(cPr)₂,

- R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 15 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 20 15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 25 20 a compound of Formula (50) wherein R³ is 2-
ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is
OMe, R^{4d} is OMe and R^{4e} is H;
- 30 25 a compound of Formula (50) wherein R³ is cyclobutyl-
amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- 35 30 a compound of Formula (50) wherein R³ is
N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 40 35 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,

- R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 25 20 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃, R^{4a} is Br, R^{4b} is H, R^{4c} is
OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
F and R^{4e} is H;
- 35 35 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

5

a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH₂CH₃), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

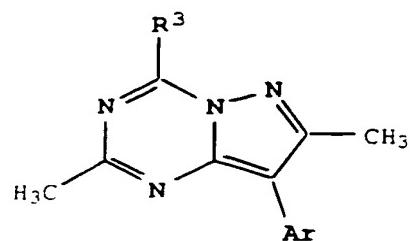
15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H; and

25 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H.

25

[2] The present invention also provides compounds of Formula (60)



30

FORMULA (60)

and isomers thereof, stereoisomeric forms thereof, or

mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, selected from the group:

- 5 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 35 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 40 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 45 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is
N(Et)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
yl;

20 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃, Ar is 6-dimethylamino-4-

methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

5

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

25

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is

- 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is
NH(CH₂CH₃)CH(CH₃)CH₃, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
yl;
- 25 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-

- CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 15 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-dimethylamino-4-methylpyrid-3-yl.
- a compound of Formula (60) wherein R³ is 2-
20 ethylpiperid-1-yl, Ar is 6-methoxy-4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 25 25 a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 6-methoxy-4-methylpyrid-3-
yl;
- 30 30 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 6-methoxy-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 6-methoxy-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-methoxy-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6-methoxy-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6-methoxy-4-methylpyrid-3-
yl;
- 20 a compound of Formula (60) wherein R³ is
N(Et)propargyl, Ar is 6-methoxy-4-methylpyrid-3-
yl;
- a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 6-methoxy-4-
methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-methoxy-4-methylpyrid-3-
yl;
- a compound of Formula (60) wherein R³ is

N(CH₂CH₂OMe)Et, Ar is 6-methoxy-4-methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
10 CH₂cPr, Ar is 6-methoxy-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH₂CH₃, Ar is 6-methoxy-4-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-methoxy-4-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar
is 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
30 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 4-methoxy-6-methylpyrid-3-yl;

35 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 4-methoxy-6-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
4-methoxy-6-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
4-methoxy-6-methylpyrid-3-yl;
- 20 20 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
25 NHCH(CH₃)CH(CH₃)CH₃, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 4-methoxy-6-methylpyrid-3-

yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 4-methoxy-6-methylpyrid-3-
5 yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 4-methoxy-6-methylpyrid-3-
y1;

10

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 4-methoxy-6-methylpyrid-3-
yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 4-methoxy-6-methylpyrid-3-yl;

20

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 4-methoxy-6-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
4-methoxy-6-methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 4,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
4,6-dimethylpyrid-3-yl;
15
- a compound of Formula (60) wherein R³ is N(Me)Et Ar is
4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
20 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is
N(Et)propargyl, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 4,6-dimethylpyrid-3-yl;
30
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
15 NHCH(CH₃)CH₂CH₃, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 4,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar
is 4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is 2-
30 ethylpiperid-1-yl, Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is cyclobutyl-

- amino, Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
10 Ar is Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
2,6-dimethylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
2,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
25 NH(CH(CH₃)CH(CH₃)CH₃), Ar is 2,6-dimethylpyrid-3-
yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 2,6-dimethylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 2,6-dimethylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 2,6-dimethyl pyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
15 is 2,6-dimethyl pyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 2,6-dimethylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 2,6-dimethyl-pyrid-3-yl; and

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
2,6-dimethyl-pyrid-3-yl.

25 [3] Specifically preferred compounds of the present
invention include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
30 acceptable salt forms thereof, wherein said compound
is selected from the group:

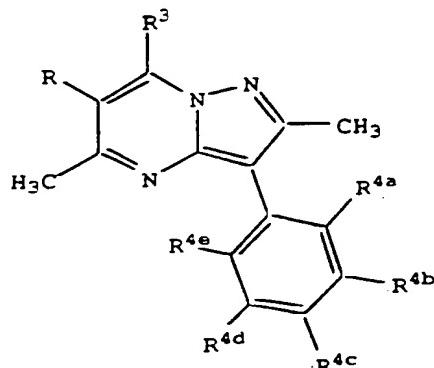
4-((2-butyl)amino)-2,7-dimethyl-8-(2-methyl-4-

- methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 4-((2-butyl)amino)-2,7-dimethyl-8-(2,5-di methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 5
4-((3-pentyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 10
4-((3-pentyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 15
4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 20
4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 25
4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 30
4-(diallylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 4-(diallylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 35
4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-

triazine; and

4 - (N-ethyl-N- (2-methoxyethyl) amino) -2,7-dimethyl-8-
 (2,5-dimethyl-4-methoxyphenyl) -[1,5-a] -pyrazolo-
 5 1,3,5-triazine.

[4] The present invention further provides
 compounds of Formula (70)



10

FORMULA (70)

15 and isomers thereof, stereoisomeric forms thereof, or
 mixtures of stereoisomeric forms thereof, and
 pharmaceutically acceptable salt forms thereof selected
 from the group:

20 a compound of Formula (70) wherein R is Cl, R³ is -
 NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d}
 is H and R^{4e} is H;

25 a compound of Formula (70) wherein R is Cl, R³ is -
 NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d}
 is H and R^{4e} is H;

a compound of Formula (70) wherein R is Cl, R³ is -
 N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d}
 30 is H and R^{4e} is H;

- a compound of Formula (70) wherein R is Cl, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is -(S)-

- NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is - NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is - N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is (S) - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is

- Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is - N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is Cl, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is -

- NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is - NET₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H; and
- 15 a compound of Formula (70) wherein R is Cl, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is (S)- NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is Me, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -N(c-

- Pr) (CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is -NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is

- is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R^3 is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R^3 is - N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 15 a compound of Formula (70) wherein R is Me, R^3 is - NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 20 a compound of Formula (70) wherein R is Me, R^3 is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 25 a compound of Formula (70) wherein R is Me, R^3 is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 30 a compound of Formula (70) wherein R is Me, R^3 is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 35 a compound of Formula (70) wherein R is Me, R^3 is - NET₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H; and
- 40 40 a compound of Formula (70) wherein R is Me, R^3 is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is F, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -N(n-Bu)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is -

- NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 15 a compound of Formula (70) wherein R is F, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

- Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R^3 is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R^3 is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R^3 is -(S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R^3 is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R^3 is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R^3 is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R^3 is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R^3 is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is - N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is - N(Bu)(Et), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is - N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is Cl, R³ is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H

- and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R^3 is - NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R^3 is - NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R^3 is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R^3 is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R^3 is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R^3 is - N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R^3 is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R^3 is - NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me

and R^{4e} is H;

5 a compound of Formula (70) wherein R is Cl, R^3 is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

10 a compound of Formula (70) wherein R is Cl, R^3 is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is ME and R^{4e} is H;

15 a compound of Formula (70) wherein R is F, R^3 is -N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (70) wherein R is F, R^3 is -N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (70) wherein R is F, R^3 is -N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (70) wherein R is F, R^3 is -NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (70) wherein R is F, R^3 is -NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (70) wherein R is F, R^3 is -NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (70) wherein R is F, R^3 is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (70) wherein R is F, R^3 is cyclobutylaminc, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,

- R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 15 a compound of Formula (70) wherein R is F, R³ is - N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 20 a compound of Formula (70) wherein R is F, R³ is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 25 a compound of Formula (70) wherein R is F, R³ is - NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is - NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 35 a compound of Formula (70) wherein R is F, R³ is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 40 a compound of Formula (70) wherein R is Me, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is Me, R³ is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H.

- a compound of Formula (70) wherein R is Me, R³ is - N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is - NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is - NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is - 2-buty1, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

a compound of Formula (70) wherein R is Me, R³ is -NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

5

a compound of Formula (70) wherein R is Me, R³ is -NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

10 a compound of Formula (70) wherein R is Me, R³ is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H; and

15 a compound of Formula (70) wherein R is Me, R³ is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H.

[5] Specifically preferred compounds of the present invention include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, wherein said compound is selected from: 7-(diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]-pyrazolopyrimidine and 7-(N-(3-cyanopropyl)-N-propylamino)-2,5-dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine.

[6] The present invention also provides pharmaceutical compositions comprising a therapeutically effective amount of the above-described compounds and a pharmaceutically acceptable carrier.

35 [7] The present invention still further provides methods of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-

traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, 5 hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals comprising administering to the mammal a therapeutically effective amount of the 10 above-described compounds.

Many compounds of this invention have one or more asymmetric centers or planes. Unless otherwise indicated, all chiral (enantiomeric and diastereomeric) and racemic forms are included in the present 20 invention. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds, and all such stable isomers are contemplated in the present invention. The compounds may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. All chiral, (enantiomeric and diastereomeric) and 25 racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomer form is specifically indicated.

The term "alkyl" includes both branched and 30 straight-chain alkyl having the specified number of

carbon atoms. Commonly used abbreviations have the following meanings: Me is methyl, Et is ethyl, Pr is propyl, Bu is butyl. The prefix "n" means a straight chain alkyl. The prefix "c" means a 5 cycloalkyl. The prefix "(S)" means the S enantiomer and the prefix "(R)" means the R enantiomer.

"Alkenyl" includes hydrocarbon chains of either a straight or branched configuration and one or more unsaturated carbon-carbon bonds which may occur in 10 any stable point along the chain, such as ethenyl, propenyl, and the like. "Alkynyl" includes hydrocarbon chains of either a straight or branched configuration and one or more triple carbon-carbon bonds which may occur in any stable point along the 15 chain, such as ethynyl, propynyl and the like.

"Haloalkyl" is intended to include both branched and straight-chain alkyl having the specified number of carbon atoms, substituted with 1 or more halogen; "alkoxy" represents an alkyl group of indicated 20 number of carbon atoms attached through an oxygen bridge; "cycloalkyl" is intended to include saturated ring groups, including mono-, bi- or poly-cyclic ring systems, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and so forth. 25 "Halo" or "halogen" includes fluoro, chloro, bromo, and iodo.

The term "substituted", as used herein, means that one or more hydrogen on the designated atom is replaced with a selection from the indicated group, 30 provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

35 Combinations of substituents and/or variables

are permissible only if such combinations result in stable compounds. By "stable compound" or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of 5 purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

The term "appropriate amino acid protecting group" means any group known in the art of organic synthesis for the protection of amine or carboxylic acid groups. Such amine protecting groups include 10 those listed in Greene and Wuts, "Protective Groups in Organic Synthesis" John Wiley & Sons, New York (1991) and "The Peptides: Analysis, Synthesis, Biology, Vol. 3, Academic Press, New York (1981), 15 the disclosure of which is hereby incorporated by reference. Any amine protecting group known in the art can be used. Examples of amine protecting groups include, but are not limited to, the following: 1) acyl types such as formyl, 20 trifluoroacetyl, phthalyl, and p-toluenesulfonyl; 2) aromatic carbamate types such as benzyloxycarbonyl (Cbz) and substituted benzyloxycarbonyls, 1-(p-biphenyl)-1-methylethoxycarbonyl, and 9-fluorenylmethyloxycarbonyl (Fmoc); 3) aliphatic 25 carbamate types such as tert-butyloxycarbonyl (Boc), ethoxycarbonyl, diisopropylmethoxycarbonyl, and allyloxycarbonyl; 4) cyclic alkyl carbamate types such as cyclopentyloxycarbonyl and adamantlyloxycarbonyl; 5) alkyl types such as triphenylmethyl and benzyl; 6) trialkylsilane such 30 as trimethylsilane; and 7) thiol containing types such as phenylthiocarbonyl and dithiasuccinoyl.

The term "pharmaceutically acceptable salts" includes acid or base salts of the compounds of 35 Formulae (1) and (2). Examples of pharmaceutically

acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like.

5 Pharmaceutically acceptable salts of the compounds of the invention can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic
10 solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing
15 Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are considered to be any covalently bonded carriers which release the active parent drug of formula (I) or (II) *in vivo* when such prodrug is
20 administered to a mammalian subject. Prodrugs of the compounds of formula (I) and (II) are prepared by modifying functional groups present in the compounds in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*,
25 to the parent compounds. Prodrugs include compounds wherein hydroxy, amine, or sulfhydryl groups are bonded to any group that, when administered to a mammalian subject, cleaves to form a free hydroxyl, amino, or sulfhydryl group, respectively. Examples
30 of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of formulas (I) and (II); and the like.

The term "therapeutically effective amount" of
35 a compound of this invention means an amount

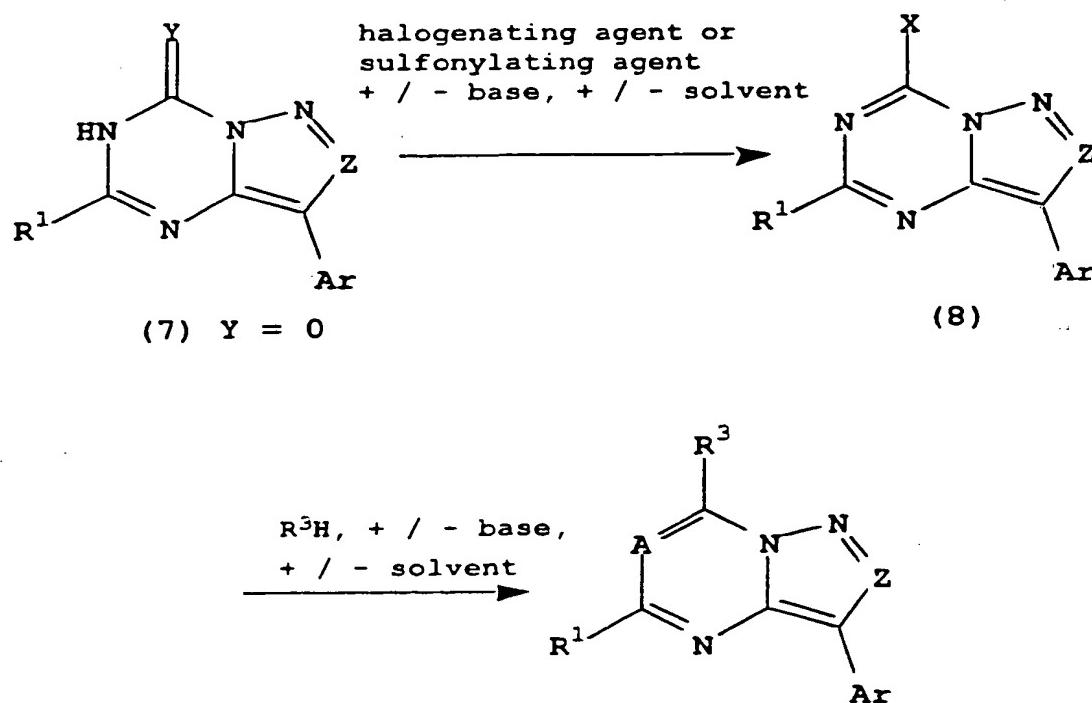
effective to antagonize abnormal level of CRF or treat the symptoms of affective disorder, anxiety or depression in a host.

5

Syntheses

Some compounds of Formula (1) may be prepared from intermediate compounds of Formula (7), using the 10 procedures outlined in Scheme 1:

SCHEME 1



(1) $A = N$
 Compounds of Formula (7) (where Y is O) may be treated with a halogenating agent or sulfonylating agent in the presence or absence of a base in the presence or 15 absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to give products of Formula (8) (where X is halogen, alkanesulfonyloxy,

arylsulfonyloxy or haloalkane-sulfonyloxy). Halogenating agents include, but are not limited to, SOCl_2 , POCl_3 , PCl_3 , PCl_5 , POBr_3 , PBr_3 or PBr_5 . Sulfonating agents include, but are not limited to, 5 alkanesulfonyl halides or anhydrides (such as methanesulfonyl chloride or methanesulfonic acid anhydride), arylsulfonyl halides or anhydrides (such as p-toluenesulfonyl chloride or anhydride) or haloalkylsulfonyl halides or anhydrides (preferably trifluoromethanesulfonic anhydride). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal 10 dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trimethylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides 15 (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) 20 or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20°C to 100°C.

Compounds of Formula (8) may be reacted with compounds of Formula R^3H (where R^3 is defined as above except R^3 is not SH , COR^7 , CO_2R^7 , aryl or heteroaryl)

in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80 to 250°C to generate compounds of Formula (1). Bases may include, but are not limited to,

5 alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates,

10 alkali metal bicarbonates, alkali metal bis(trimethylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but

15 are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-

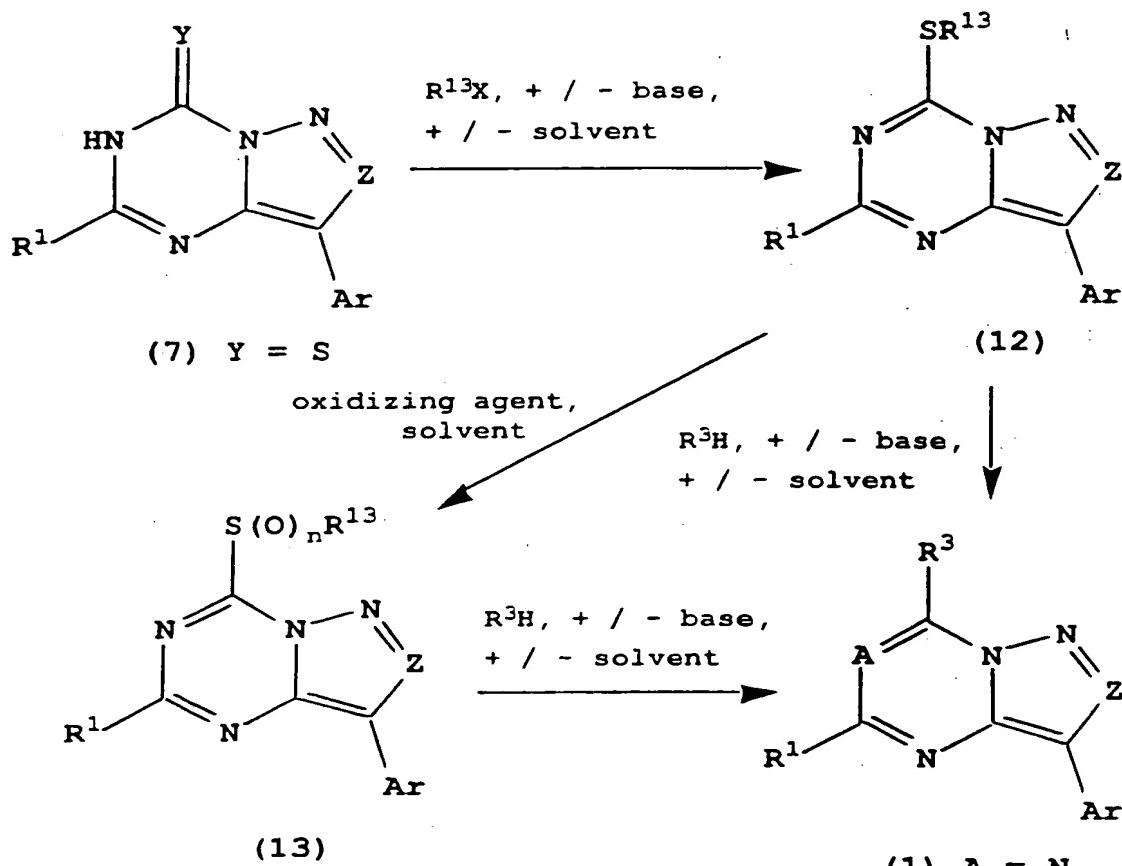
20 dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene)

25 or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from 0°C to 140°C.

Scheme 2 delineates the procedures for converting intermediate compounds of Formula (7) (where Y is S) to

30 some compounds of Formula (1).

SCHEME 2



Compounds of Formula (7) (where Y is S) may be treated with an alkylating agent $R^{13}X$ (where R^{13} is defined as above, except R^{13} is not aryl or heteroaryl) in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C . Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably

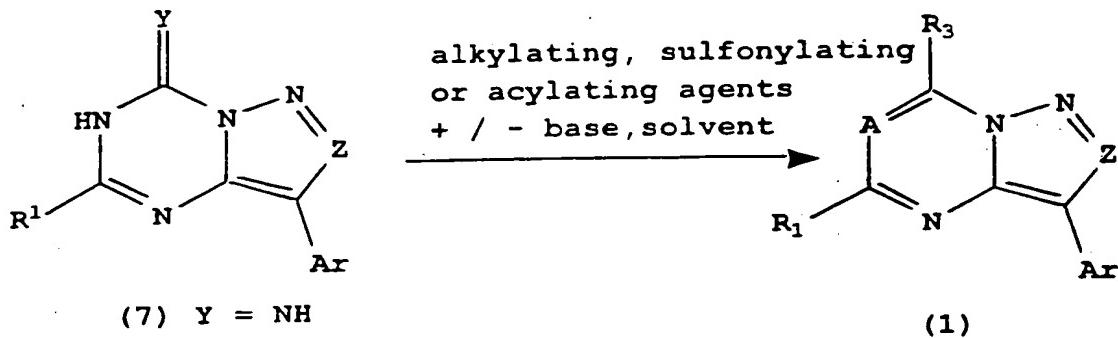
sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -80°C to 100°C.

Compounds of Formula (12) (Formula (1) where R³ is SR¹³) may then be reacted with compounds of Formula R³H to give compounds of Formula (1), using the same conditions and reagents as were used for the conversion of compounds of Formula (8) to compounds of Formula (1) as outlined for Scheme 1 above. Alternatively, compounds of Formula (12) (Formula (1) where R³ is SR¹³) may be oxidized to compounds of Formula (13) (Formula (1) where R³ is S(O)_nR¹³, n is 1,2) by treatment with an oxidizing agent in the presence of an inert solvent at temperatures ranging from -80°C to 250°C. Oxidizing agents include, but are not limited to, hydrogen peroxide, alkane or aryl peracids (preferably peracetic acid or m-chloro-perbenzoic acid), dioxirane, oxone, or sodium periodate. Inert solvents may include, but are not limited to, alkanones (3 to 10 carbons, preferably acetone), water, alkyl

alcohols (1 to 6 carbons), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane) or combinations thereof. The choices 5 of oxidant and solvent are known to those skilled in the art (cf. Uemura, S., Oxidation of Sulfur, Selenium and Tellurium, in Comprehensive Organic Synthesis, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 7, 762-769). Preferred reaction temperatures range from 10 -20°C to 100°C. Compounds of Formula (13) (Formula (1) where R³ is S(O)_nR¹³, n is 1,2) may then be reacted with compounds of Formula R³H to give compounds of Formula 15 (1), using the same conditions and reagents as were used for the conversion of compounds of Formula (8) to compounds of Formula (1) as outlined for Scheme (1) above.

Compounds of Formula (1), where R³ may be - NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, - 20 NR⁸SO₂R⁷, may be prepared from compounds of Formula (7), where Y is NH, by the procedures depicted in Scheme 3.

SCHEME 3



$\mathbf{A} = \mathbf{N};$
 $\mathbf{R}^3 = \mathbf{NR}^6\mathbf{R}^7, \mathbf{NR}^8\mathbf{COR}^7,$
 $\mathbf{N}(\mathbf{COR}^7)_2, \mathbf{NR}_8\mathbf{CONR}^6\mathbf{R}^7$
 $\mathbf{NR}_8\mathbf{CO}_2\mathbf{R}_{13}$

Reaction of compounds of Formula (7), where Y is NH, with alkylating agents, sulfonylating agents or acylating agents or sequential reactions with combinations thereof, in the presence or absence of a base in an inert solvent at reaction temperatures ranging from -80°C to 250°C may afford compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, -NR⁸SO₂R⁷. Alkylating agents may include, but are not limited to, C₁-C₁₀ alkyl-halides, -tosylates, -mesylates or -triflates; C₁-C₁₀ haloalkyl(1 - 10 halogens)-halides, -tosylates, -mesylates or -triflates; C₂-C₈ alkoxyalkyl-halides, -tosylates, -mesylates or -triflates; C₃-C₆ cycloalkyl-halides, -tosylates, -mesylates or -triflates; C₄-C₁₂ cycloalkylalkyl-halides, -tosylates, -mesylates or -triflates; aryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; heteroaryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; or heterocyclyl(C₁-C₄ alkyl)-halides, -tosylates, -

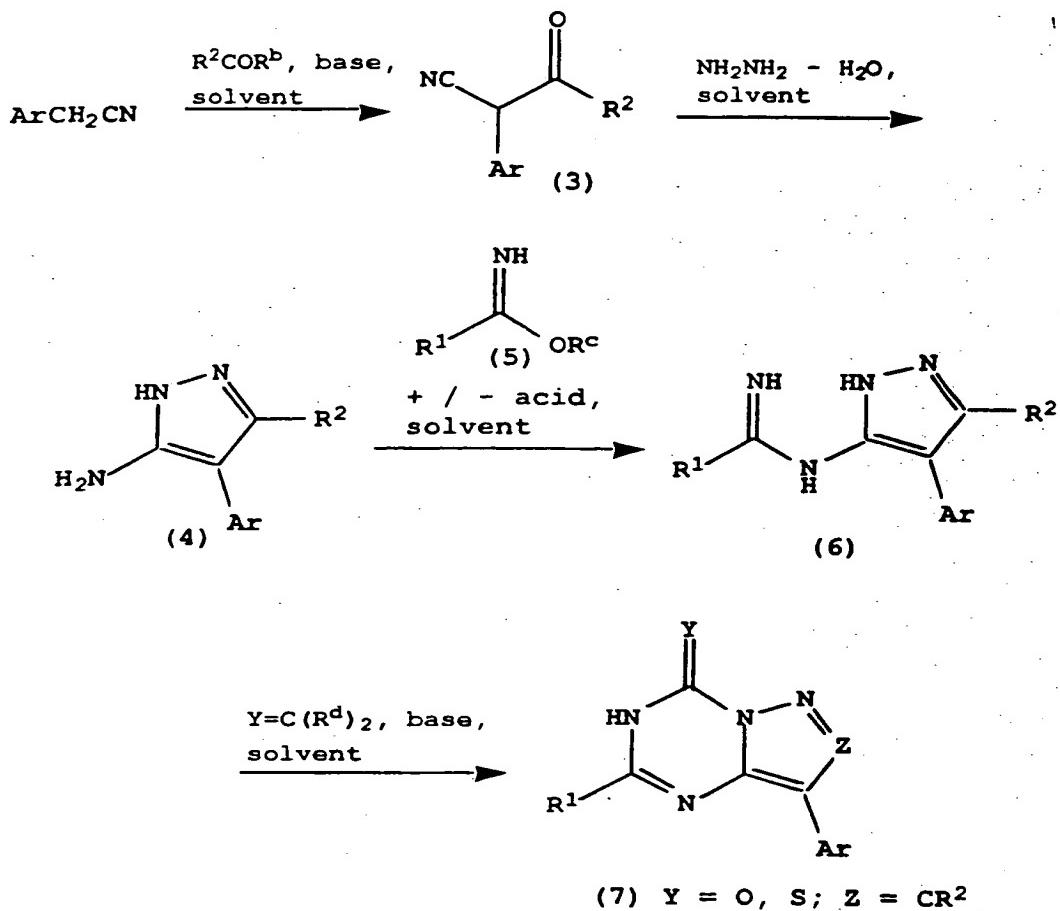
mesylates or -triflates. Acylating agents may include, but are not limited to, C₁-C₁₀ alkanoyl halides or anhydrides, C₁-C₁₀ haloalkanoyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkanoyl halides or anhydrides, C₃-C₆ cycloalkanoyl halides or anhydrides, C₄-C₁₂ cycloalkylalkanoyl halides or anhydrides, aroyl halides or anhydrides, aryl(C₁-C₄) alkanoyl halides or anhydrides, heteroaroyl halides or anhydrides, heteroaryl(C₁-C₄) alkanoyl halides or anhydrides, heterocyclcarboxylic acid halides or anhydrides or heterocycl(C₁-C₄) alkanoyl halides or anhydrides.

Sulfonylating agents include, but are not limited to, C₁-C₁₀ alkylsulfonyl halides or anhydrides, C₁-C₁₀ haloalkylsulfonyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkylsulfonyl halides or anhydrides, C₃-C₆ cycloalkylsulfonyl halides or anhydrides, C₄-C₁₂ cycloalkylalkylsulfonyl halides or anhydrides, arylsulfonyl halides or anhydrides, aryl(C₁-C₄ alkyl)-, heteroarylsulfonyl halides or anhydrides, heteroaryl(C₁-C₄ alkyl)sulfonyl halides or anhydrides, heterocyclsulfonyl halides or anhydrides or heterocycl(C₁-C₄ alkyl)sulfonyl halides or anhydrides. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower

alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably 5 dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures 10 range from 0°C to 100°C.

Scheme 4 delineates procedures, which may be employed to prepare intermediate compounds of Formula (7), where Y is O, S and Z is CR².

SCHEME 4



Compounds of the formula $ArCH_2CN$ are reacted with compounds of the formula R^2COR^b , where R^2 is defined above and R^b is halogen, cyano, lower alkoxy (1 to 6 carbons) or lower alkanoyloxy (1 to 6 carbons), in the presence of a base in an inert solvent at reaction temperatures ranging from $-78^\circ C$ to $200^\circ C$ to afford compounds of Formula (3). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal

dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), water, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.

Compounds of Formula (3) may be treated with hydrazine-hydrate in the presence of an inert solvent at temperatures ranging from 0°C to 200°C, preferably 70°C to 150°C, to produce compounds of Formula (4). Inert solvents may include, but are not limited to, water, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Compounds of Formula (4) may be reacted with compounds of Formula (5) (where R^c is alkyl (1-6 carbons)) in the

presence or absence of an acid in the presence of an inert solvent at temperatures ranging from 0°C to 200°C to produce compounds of Formula (6). Acids may include, but are not limited to alkanoic acids of 2 to 5 10 carbons (preferably acetic acid), haloalkanoic acids (2 - 10 carbons, 1-10 halogens, such as trifluoroacetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), 10 hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may be used. Inert solvents may include, but are not limited to, water, alkanenitriles (1 to 6 carbons, preferably acetonitrile), halocarbons of 1 to 6 carbons 15 and 1 to 6 halogens (preferably dichloromethane or chloroform), alkyl alcohols of 1 to 10 carbons (preferably ethanol), dialkyl ethers (4 to 12 carbons, preferably diethyl ether or di-isopropylether) or cyclic ethers such as dioxan or tetrahydrofuran.

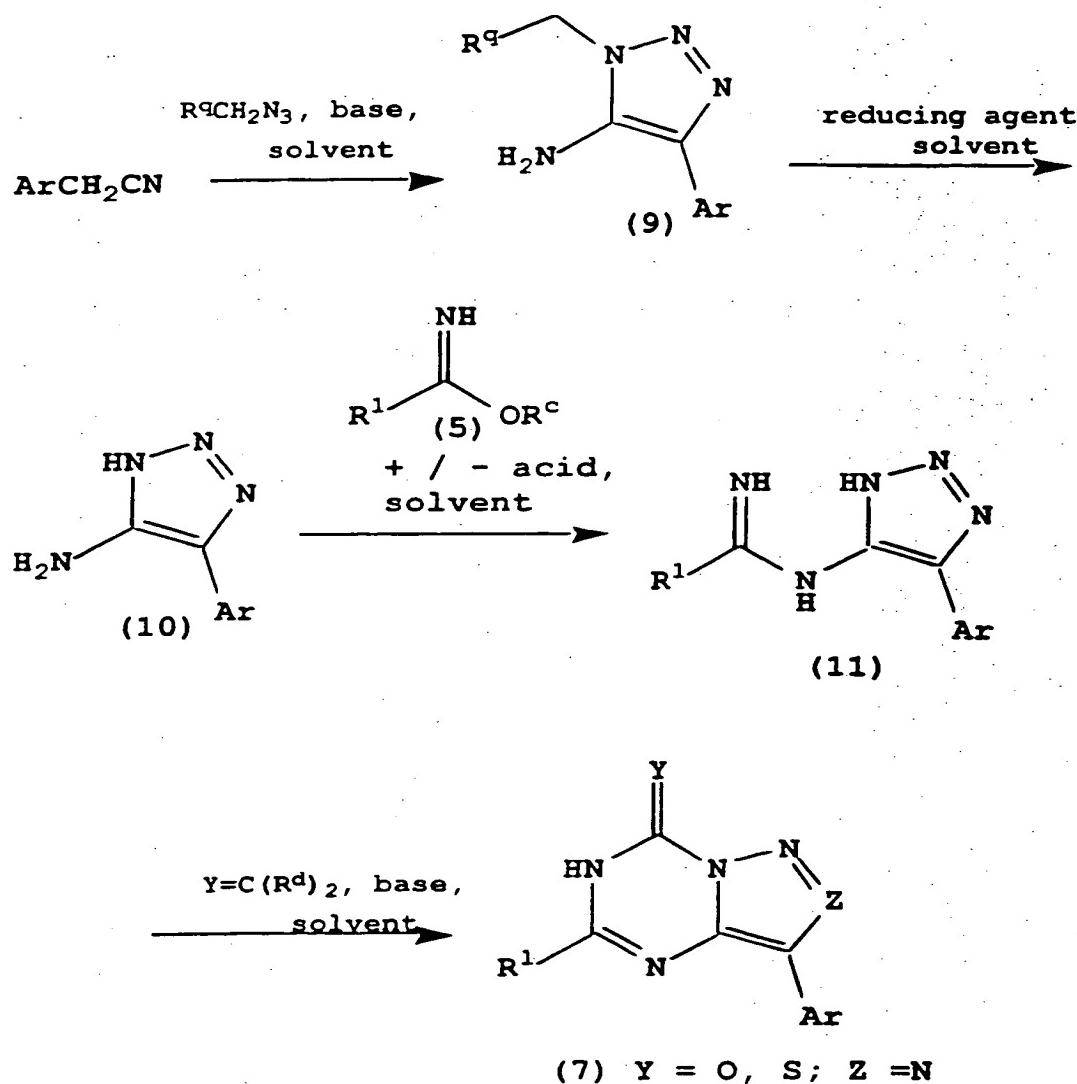
20 Preferred temperatures range from ambient temperature to 100°C.

Compounds of Formula (6) may be converted to intermediate compounds of Formula (7) by treatment with compounds $C=Y(R^d)_2$ (where Y is O or S and R^d is halogen 25 (preferably chlorine), alkoxy (1 to 4 carbons) or alkylthio (1 to 4 carbons)) in the presence or absence of a base in an inert solvent at reaction temperatures from -50°C to 200°C. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium 30 hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkali metal carbonates, alkali metal hydroxides, trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic 35 amines (preferably pyridine). Inert solvents may

include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred temperatures are 0°C to 150°C.

Intermediate compounds of Formula (7), where Z is N, may be synthesized according the methods outlined in Scheme 5.

SCHEME 5



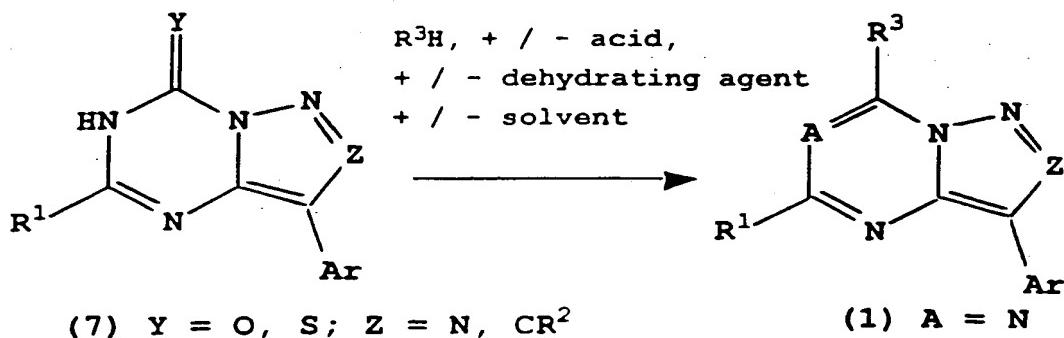
Compounds of ArCH_2CN are reacted with compounds of Formula $\text{R}^q\text{CH}_2\text{N}_3$ (where R^q is a phenyl group optionally substituted by H, alkyl (1 to 6 carbons) or alkoxy (1 to 6 carbons) in the presence or absence of a base in an inert solvent at temperatures ranging from 0°C to 200°C to generate compounds of Formula (9). Bases may

include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide, sodium ethoxide or potassium t-butoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from ambient temperature to 100°C. Compounds of Formula (9) may be treated with a reducing agent in an inert solvent at -100°C to 100°C to afford products of Formula (10). Reducing agents include, but are not limited to, (a) hydrogen gas in combination with noble metal catalysts such as Pd-on-carbon, PtO₂, Pt-on-carbon, Rh-on-alumina or Raney nickel, (b) alkali metals (preferably sodium) in combination with liquid ammonia or (c) ceric ammonium nitrate. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), water, dialkyl ethers (preferably

diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). The preferred reaction temperatures are -50°C to 60°C. Compounds of Formula (9) are then converted to compounds of Formula (7) (where Z is N) via intermediates of Formula (11) using the reagents and reaction conditions outlined in Scheme 4 for the conversion of compounds of Formula (4) to compounds of Formula (7) (where Z is CR²).

Compounds of Formula (1) may also be prepared from compounds of Formula (7) (where Y is O, S and Z is defined above) as outlined in Scheme 6:

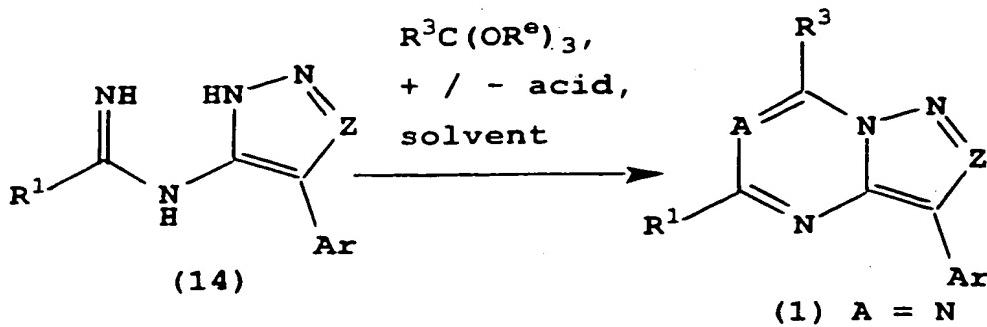
SCHEME 6



Compounds of Formula (7) may be reacted with compounds of Formula R³H in the presence of a dehydrating agent in an inert solvent at reaction temperatures ranging from 0°C to 250°C. Dehydrating agents include, but are not limited to, P₂O₅, molecular sieves or inorganic or organic acids. Acids may include, but are not limited to alcanoic acids of 2 to 10 carbons (preferably acetic

- acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid.
- 5 Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably glyme or diglyme), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide),
- 10 aromatic hydrocarbons (preferably benzene or toluene) or halocarbons of 1 to 10 carbons and 1 to 10 halogens (preferably chloroform). Preferred reaction temperatures range from ambient temperature to 150°C.
- 15 Some compounds of Formula (1) (where A is N) may also be prepared by the methods shown in Scheme 7:

SCHEME 7

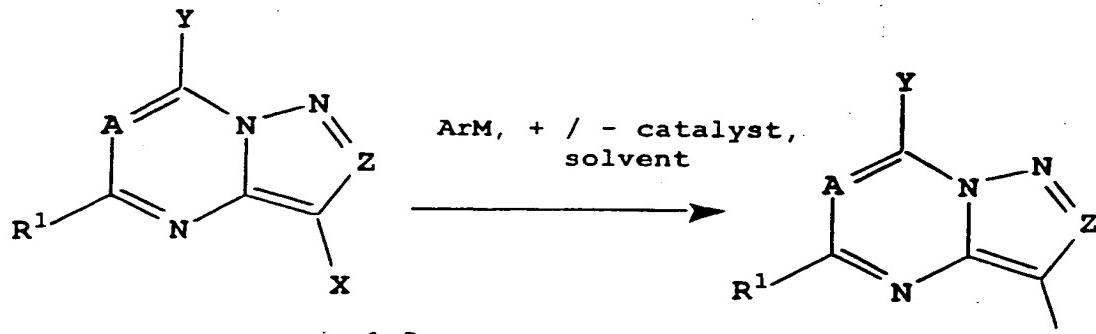


- Intermediate compounds of Formula (14), where Z is defined above, may be reacted with compounds of Formula
- 25 R³C(OR⁹)₃, where R⁹ may be alkyl (1 to 6 carbons) in the presence or absence of an acid in an inert solvent at temperatures ranging from 0°C to 250°C. Acids may

include, but are not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may be used. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably 5) acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from 50°C to 150°C.

Intermediate compounds of Formula (7) may also be synthesized by the reactions displayed in Scheme 8.

SCHEME 8



15) Y = OH, SH NR⁶R⁷;

Z = N, CR²,

X = Br, Cl, I, B(OR'')₂

(7) A = N

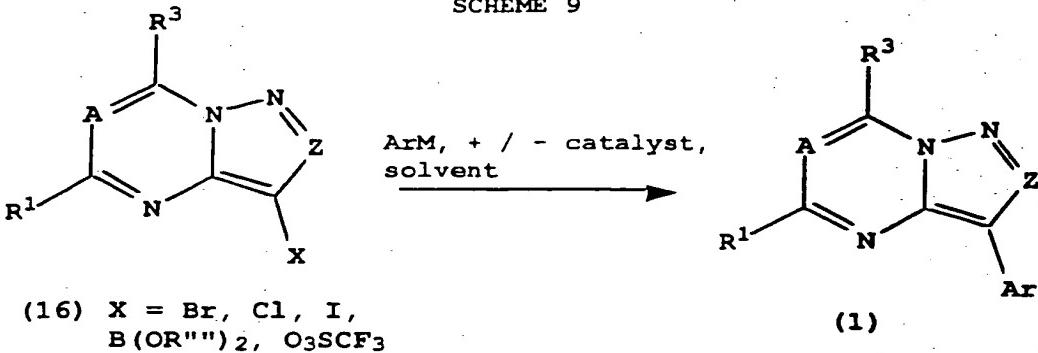
Compounds of Formula (15), (where Y is OH, SH, NR⁶R⁷; Z is defined above, X is Br, Cl, I, O₃SCF₃ or B(OR'')₂ and R''' is H or alkyl (1 to 6 carbons)) may be reacted with a compound of Formula ArM (where M is halogen, 5 alkali metal, ZnCl, ZnBr, ZnI, MgBr, MgCl, MgI, CeCl₂, CeBr₂ or copper halides) in the presence or absence of an organometallic catalyst in the presence or absence of a base in an inert solvents at temperatures ranging from -100°C to 200°C. Those skilled in the art will 10 recognize that the reagents ArM may be generated in situ. Organometallic catalysts include, but are not limited to, palladium phosphine complexes (such as Pd(PPh₃)₄), palladium halides or alkanoates (such as PdCl₂(PPh₃)₂ or Pd(OAc)₂) or nickel complexes (such as 15 NiCl₂(PPh₃)₂). Bases may include, but are not limited to, alkali metal carbonates or trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine). Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl 20 ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably 25 dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or water. Preferred reaction temperatures range from -80°C to 100°C.

The choices of M and X are known to those skilled in the art (cf. Imamoto, T., *Organocerium Reagents in 30 Comprehensive Organic Synthesis*, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 1, 231-250; Knochel, P., *Organozinc, Organocadmium and Organomercury Reagents in Comprehensive Organic Synthesis*, Trost, B.M. ed., (Elmsford, NY: Pergamon

Press, 1991), 1, 211-230; Knight, D.W., Coupling Reactions between sp^2 Carbon Centers, in Comprehensive Organic Synthesis, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 3, 481-520).

- 5 Compounds of Formula (1) may also be prepared using the methods shown in Scheme 9.

SCHEME 9



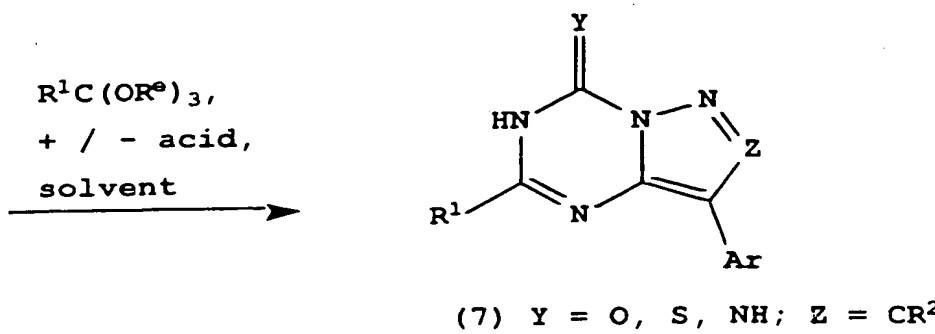
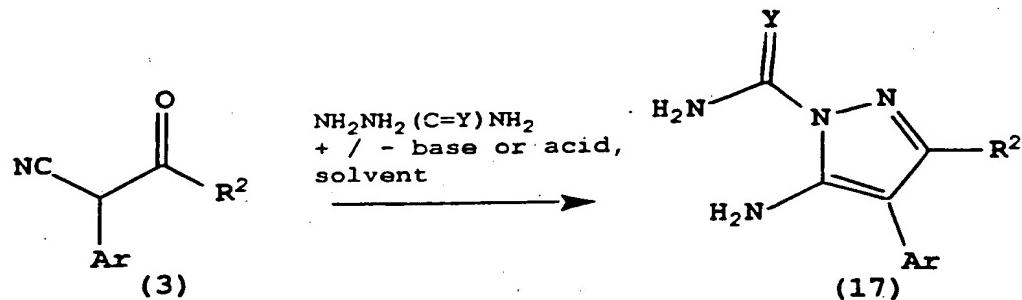
- 10 Compounds of Formula (16), where A, Z, R¹ and R³ are defined above and X is Br, Cl, I, O₃SCF₃ or B(OR'')₂ and R'' is H or alkyl (1 to 6 carbons)) may be reacted with a compound of Formula ArM (where M is halogen, alkali metal, ZnCl, ZnBr, ZnI, MgBr, MgCl, MgI, CeCl₂, CeBr₂ or copper halides) in the presence or absence of an organometallic catalyst in the presence or absence of a base in an inert solvents at temperatures ranging from -100°C to 200°C. Those skilled in the art will recognize that the reagents ArM may be generated in situ (see the above references in Comprehensive Organic Synthesis). Organometallic catalysts include, but are not limited to, palladium phosphine complexes (such as Pd(PPh₃)₄), palladium halides or alkanoates (such as PdCl₂(PPh₃)₂ or Pd(OAc)₂) or nickel complexes (such as NiCl₂(PPh₃)₂). Bases may include, but are not limited to, alkali metal carbonates or trialkyl amines

(preferably N,N-di-isopropyl-N-ethyl amine or triethylamine). Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or water. Preferred reaction temperatures range from -80°C to 100°C.

Intermediate compounds of Formula (7) (where Y is O, S, NH, Z is CR² and R¹, R² and Ar are defined as above) may be prepared as illustrated in Scheme 10.

15

SCHEME 10



Compounds of Formula (3) may be reacted with compounds

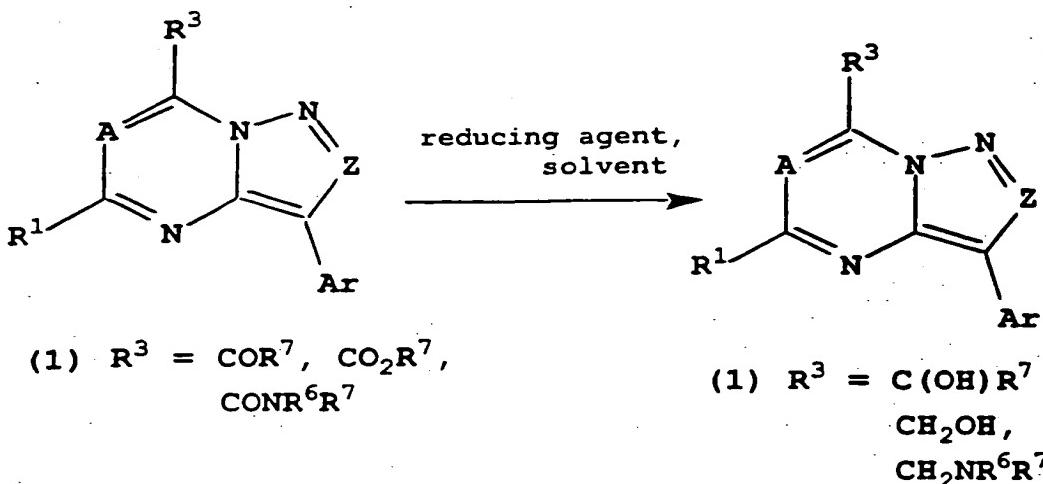
of Formula $H_2NNH(C=Y)NH_2$, where Y is O, S or NH, in the presence or absence of a base or acid in an inert solvent at temperatures from 0°C to 250°C to produce compounds of Formula (17). Acids may include, but are
5 not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid,
10 sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may be used. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium
15 ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or
20 triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or
25 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably
30 dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).

Preferred reaction temperatures range from 0°C to 150°C. Compounds of Formula (17) may then be reacted
35 with compounds of Formula $R^3C(OR^e)_3$, where R^e may be

alkyl (1 to 6 carbons) in the presence or absence of an acid in an inert solvent at temperatures ranging from 0°C to 250°C. Acids may include, but are not limited to alcanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may 5 be used. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides 10 (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) 15 or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction 20 temperatures range from 50°C to 150°C.

In Scheme 11, the procedures which may be used to convert compounds of Formula (1), where R³ is COR⁷, CO₂R⁷, NR⁸COR⁷ and CONR⁶R⁷, to other compounds of 25 Formula (1), where R³ is CH(OH)R⁷, CH₂OH, NR⁸CH₂R⁷ and CH₂NR⁶R⁷ by treatment with a reducing agent in an inert solvent at temperatures ranging from -80°C to 250°C.

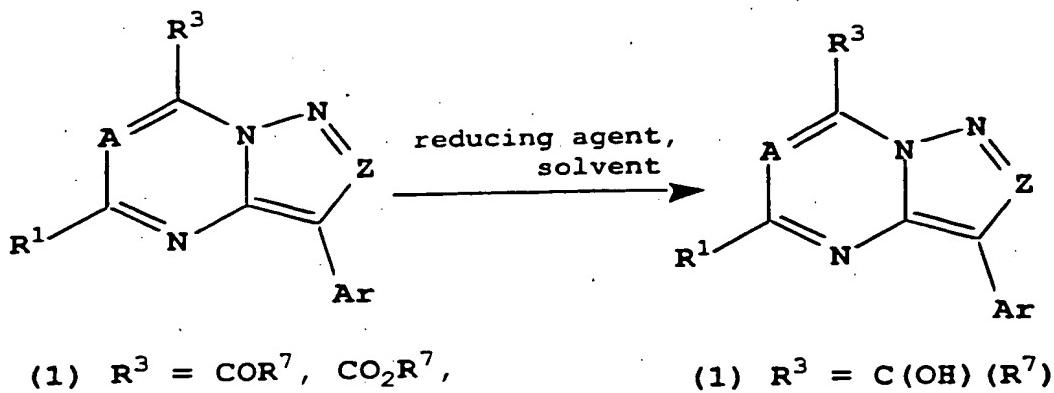
SCHEME 11



Reducing agents include, but are not limited to, alkali metal or alkaline earth metal borohydrides (preferably lithium or sodium borohydride), borane, dialkylboranes (such as di-isoamylborane), alkali metal aluminum hydrides (preferably lithium aluminum hydride), alkali metal (trialkoxy)aluminum hydrides, or dialkyl aluminum hydrides (such as di-isobutylaluminum hydride). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80°C to 100°C.

In Scheme 12, the procedures are shown which may be used to convert compounds of Formula (1), where R^3 is COR^7 or CO_2R^7 , to other compounds of Formula (1), where R^3 is $C(OH)(R^7)_2$ by treatment with a reagent of Formula R^7M in an inert solvent at temperatures ranging from -80°C to 250°C.

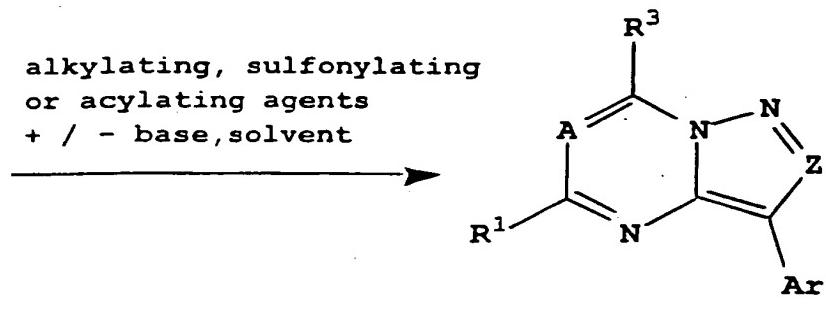
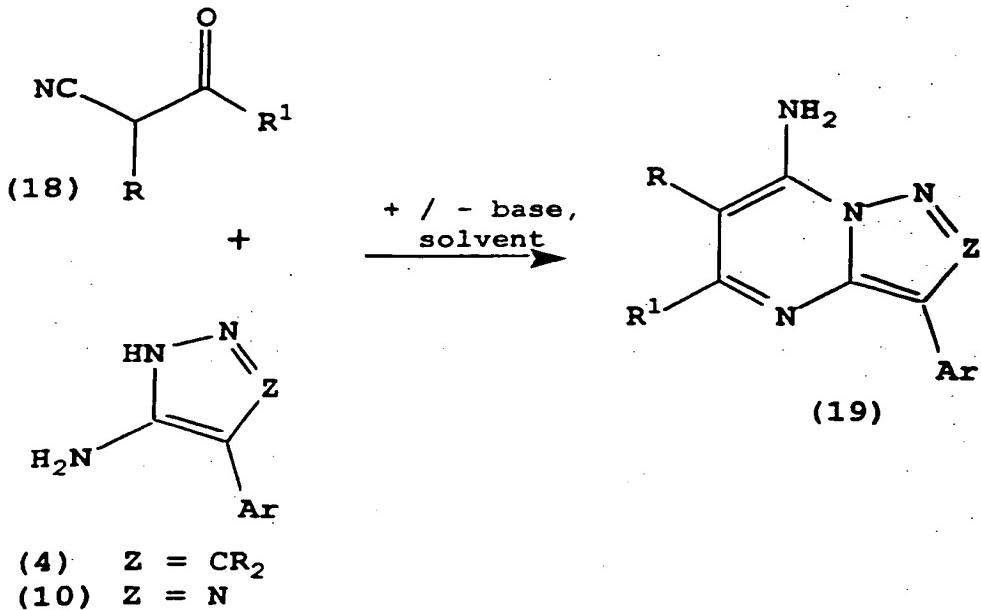
SCHEME 12



M is halogen, alkali metal, $ZnCl$, $ZnBr$, ZnI , $MgBr$,
 $MgCl$, MgI , $CeCl_2$, $CeBr_2$ or copper halides. Inert
5 solvents may include, but are not limited to, dialkyl
ethers (preferably diethyl ether), cyclic ethers
(preferably tetrahydrofuran) or aromatic hydrocarbons
(preferably benzene or toluene). Preferred reaction
temperatures range from $-80^{\circ}C$ to $100^{\circ}C$.

10 Compounds of Formula (1), where R^3 may be -
 NR^8COR^7 , $-N(COR^7)_2$, $-NR^8CONR^6R^7$, $-NR^8CO_2R^{13}$, $-NR^6R^7$, -
 $NR^8SO_2R^7$, may be synthesized as depicted in Scheme 13.

SCHEME 13



A = CR
R₃ = NR⁶R⁷, NR⁸COR⁷,
 N(COR⁷)₂,
 NR₈CONR⁶R⁷,
 NR₈CO₂R₁₃

Reaction of compounds of Formula (18), where R and R¹
 are defined above, with compounds of Formula (4) or
 5 (10) in the presence or absence of base in an inert
 solvent may produce compounds of Formula (19) at

temperatures ranging from -50°C to 250°C. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene).

Preferred reaction temperatures range from 0°C to 100°C.

Compounds of Formula (19) may then be reacted with alkylating agents, sulfonylating agents or acylating agents or sequential reactions with combinations thereof, in the presence or absence of a base in an inert solvent at reaction temperatures ranging from -80°C to 250°C may afford compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, -NR⁸SO₂R⁷. Alkylating agents may include, but are not limited to, C₁-C₁₀ alkyl -halides, -tosylates, -mesylates or -triflates; C₁-C₁₀ haloalkyl(1 - 10 halogens)-halides, -tosylates, -

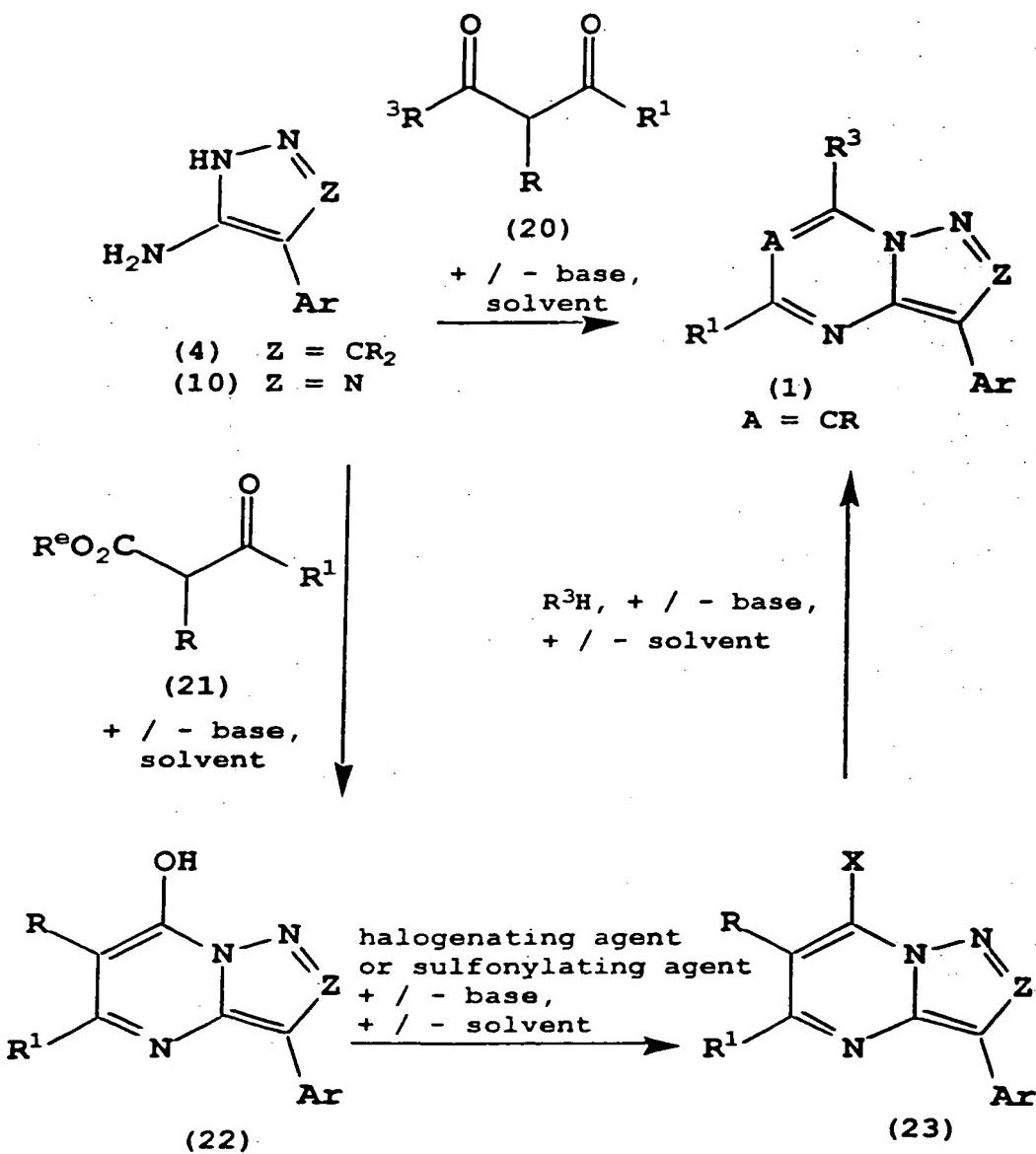
mesylates or -triflates; C₂-C₈ alkoxyalkyl-halides, -tosylates, -mesylates or -triflates; C₃-C₆ cycloalkyl-halides, -tosylates, -mesylates or -triflates; C₄-C₁₂ cycloalkylalkyl-halides, -tosylates, -mesylates or -triflates; aryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; heteroaryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; or heterocyclyl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates. Acylating agents may include, but are not limited to, C₁-C₁₀ alkanoyl halides or anhydrides, C₁-C₁₀ haloalkanoyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkanoyl halides or anhydrides, C₃-C₆ cycloalkanoyl halides or anhydrides, C₄-C₁₂ cycloalkylalkanoyl halides or anhydrides, aroyl halides or anhydrides, aryl(C₁-C₄) alkanoyl halides or anhydrides, heteroaroyl halides or anhydrides, heteroaryl(C₁-C₄) alkanoyl halides or anhydrides, heterocyclylcarboxylic acid halides or anhydrides or heterocyclyl(C₁-C₄) alkanoyl halides or anhydrides.

Sulfonylating agents include, but are not limited to, C₁-C₁₀ alkylsulfonyl halides or anhydrides, C₁-C₁₀ haloalkylsulfonyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkylsulfonyl halides or anhydrides, C₃-C₆ cycloalkylsulfonyl halides or anhydrides, C₄-C₁₂ cycloalkylalkylsulfonyl halides or anhydrides, arylsulfonyl halides or anhydrides, aryl(C₁-C₄ alkyl)-, heteroarylsulfonyl halides or anhydrides, heteroaryl(C₁-C₄ alkyl)sulfonyl halides or anhydrides, heterocyclylsulfonyl halides or anhydrides or heterocyclyl(C₁-C₄ alkyl)sulfonyl halides or anhydrides. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably

sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably 5 sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower 10 alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably 15 dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.

20 Compounds of Formula (1), where A is CR and R is defined above, may be synthesized by the methods depicted in Scheme 14.

SCHEME 14



Compounds of Formula (4) or (10) may be treated with compounds of Formula (20), where R¹ and R³ are defined above in the presence or absence of base in an inert solvent at temperatures ranging from 0°C to 250°C to give compounds of Formula (1), where A is CR and R is

defined above. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene).

Preferred reaction temperatures range from 0°C to 100°C. Alternatively, compounds of Formula (1) where A is CR and R is defined above, may be synthesized through intermediates (22) and (23).

Compounds of Formula (4) or (10) may be treated with compounds of Formula (21), where R¹ is defined above and R^e is alkyl (1 - 6 carbons), in the presence or absence of base in an inert solvent at temperatures ranging from 0°C to 250°C to give compounds of Formula (1), where A is CR and R is defined above. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide),

alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably 5 pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably 10 tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or 15 aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C. Compounds of Formula (22) may be treated with a halogenating agent or sulfonylating agent in the presence or absence of a base in the presence or 20 absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to give products of Formula (23) (where X is halogen, alkanesulfonyloxy, arylsulfonyloxy or haloalkane-sulfonyloxy). Halogenating agents include, but are not limited to, 25 SOCl₂, POCl₃, PCl₅, POBr₃, PBr₃ or PBr₅. Sulfonylating agents include, but are not limited to, alkanesulfonyl halides or anhydrides (such as methanesulfonyl chloride or methanesulfonic acid anhydride), arylsulfonyl halides or anhydrides (such as 30 p-toluenesulfonyl chloride or anhydride) or haloalkylsulfonyl halides or anhydrides (preferably trifluoromethanesulfonic anhydride). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium 35

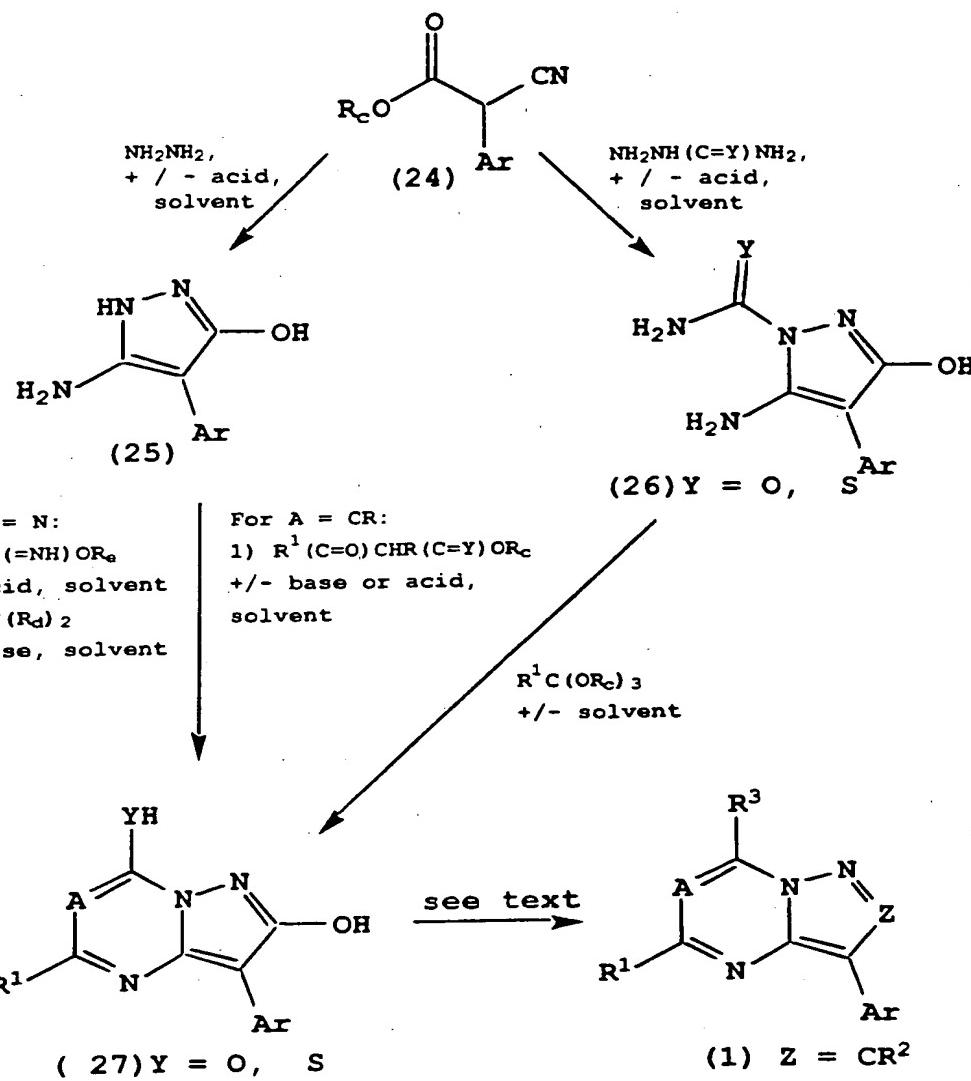
ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20°C to 100°C.

Compounds of Formula (23) may be reacted with compounds of Formula R³H (where R³ is defined as above except R³ is not SH, COR⁷, CO₂R⁷, aryl or heteroaryl) in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to generate compounds of Formula (1). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bicarbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine) or aromatic amines

(preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from 0°C to 140°C.

15 Some compounds of Formula (1) may also be prepared using the methods shown in Scheme 15.

SCHEME 15



A compound of Formula (24) (R_c is a lower alkyl group and Ar is defined as above) may be reacted with hydrazine in the presence or absence of an inert solvent to afford an intermediate of Formula (25), where Ar is defined as above. The conditions employed are similar to those used for the preparation of intermediate of Formula (4) from compound of Formula (3) in Scheme 4. Compounds of Formula (25), where A is N, may be reacted with reagents of the formula

$R^1C(=NH)OR_e$, where R^1 is defined above and R_e is a lower alkyl group) in the presence or absence of an acid in an inert solvent, followed by reaction with a compound of formula $YisC(R_d)_2$ (where Y is O or S and R_d is halogen (preferably chlorine), alkoxy (1 to 4 carbons) or alkylthio (1 to 4 carbons)) in the presence or absence of a base in an inert solvent to give compounds of Formula (27) (where A is N and Y is O, S). The conditions for these transformations are the same as those employed for the conversions of compound of Formula (4) to compound of Formula (7) in Scheme 4.

Alternatively, compounds of Formula (25), where A is CR, may be reacted with compounds of the formula $R^1(C=O)CHR(C=Y)OR_c$ (where R^1 and R are defined as above and R_c is a lower alkyl group) to give a compound of Formula (27) (where A is CR) using conditions similar to those employed for the conversion of compounds of Formula (21) to compounds of Formula (22) in Scheme 14. Intermediates of Formula (27) (where Y is O) may be treated with halogenating agents or sulfonylating agents in the presence or absence of a base in an inert solvent, followed by reaction with R^3H or R^2H in the presence or absence of a base in an inert solvent to give compounds of Formula (1) (where Z is CR^2).

It will be recognized by those skilled in the art that various combinations of halogenating agents, sulfonylating agents, R^3H or R^2H may be used in different orders of reaction sequences in Scheme 15 to afford compounds of Formula (1). For example, in some cases, it may be desirable to react compounds with stoichiometric amounts of halogenating agents or sulfonylating agents, react with R^2H (or R^3H), then repeat the reaction with halogenating agents or sulfonylating agents and react with R^3H (or R^2H) to

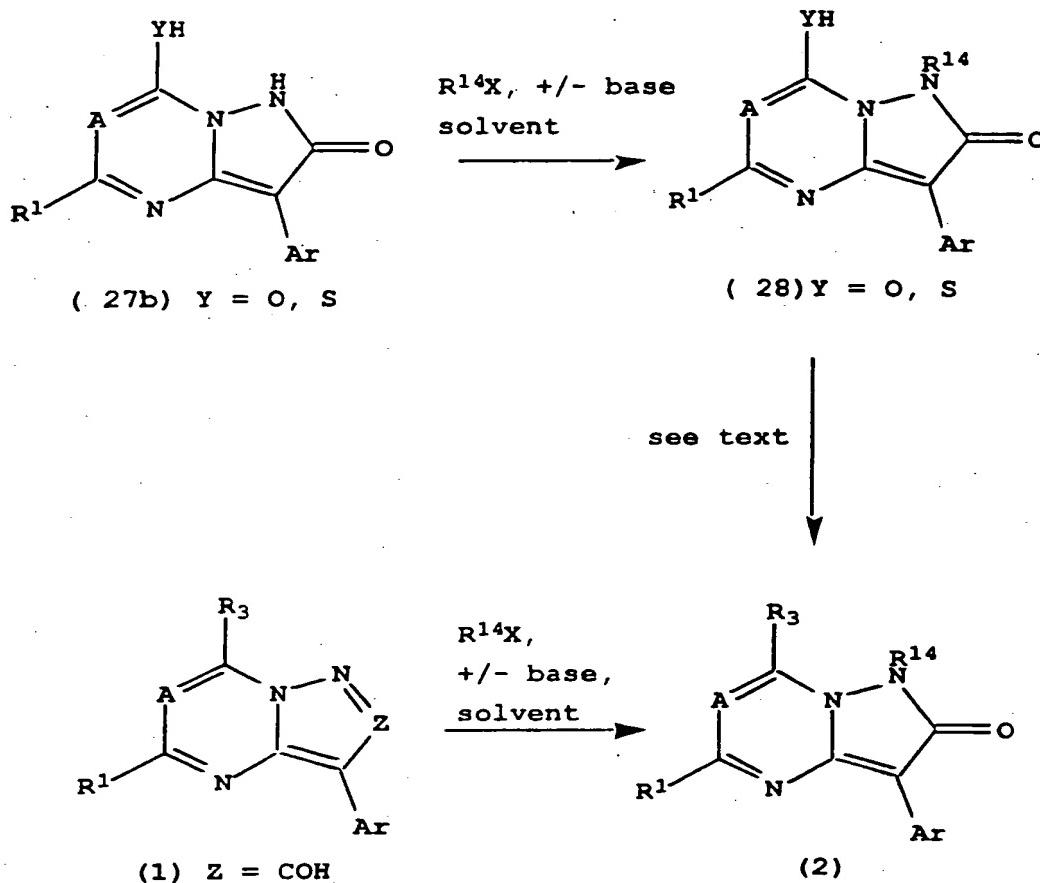
give compounds of Formula (1). The reaction conditions and reagents used for these conversions are similar to the ones employed for the conversion of intermediate compounds of Formulae (22) to (23) to (1) in Scheme 14 (for A is CR) or the conversion of intermediate compounds of Formulae (7) to (8) to (1) in Scheme 1 (where A is N).

Alternatively, compounds of Formula (27) (where Y is S) may be converted to compounds of Formula (1) in Scheme 15. Intermediate compounds of Formula (27) may be alkylated with a compound R^fX (where R^f is lower alkyl and X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in an inert solvent, (then optionally oxidized with an oxidizing agent in an inert solvent) and then reacted with R^3H in the presence or absence of a base in an inert solvent to give a compound of Formula (1). The conditions and reagents employed are similar to those used in the conversion of intermediate compounds of Formulae (7) to (12) (or to (13)) to compounds of Formula (1) in Scheme 2.

Compounds of Formula (1) may be prepared from compounds of Formula (24), using an alternate route as depicted in Scheme 15. Compounds of Formula (24) may be converted to compounds of Formula (27) via reaction with compounds of formula $NH_2NH(C=NH)NH_2$ in the presence or absence of an acid in an inert solvent, followed by reaction with compounds $R^1C(OR_c)_3$ (where R_c is lower alkyl and R^1 is defined as above), using the conditions employed for the conversion of compounds of Formulae (3) to (17) to (7) in Scheme 10.

Some compounds of Formula (2) may be prepared by the methods illustrated in Scheme 16.

SCHEME 16



Compounds of Formula (27b) may be treated with various alkylating agents $R^{14}X$ (where R^{14} is defined above and 5 X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in the presence or absence of a base in an inert solvent to afford structures of Formula (28). Compounds of Formula (28) (Y is O) may then be converted to compounds of Formula (2) by 10 treatment with halogenating agents or sulfonylating agents in the presence or absence of a base in an inert solvent, followed by reaction with R^3H in the presence or absence of a base in an inert solvent to give

compounds of Formula (2). The reaction conditions used for these conversions are similar to the ones employed for the conversion of intermediate compounds (22) to (23) to (1) in Scheme 14 (for A is CR) or the 5 conversion of intermediate compounds of Formulae (7) to (8) to (1) in Scheme 1 (where A is N). Alternatively, compounds of Formula (28) (Y is S) may be alkylated 10 with a compound R^fX (where R^f is lower alkyl and X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in an inert solvent, (then optionally oxidized with an 15 oxidizing agent in an inert solvent) and then reacted with R³H in the presence or absence of a base in an inert solvent to give a compound of Formula (1). The conditions and reagents employed are similar to those 20 used in the conversion of intermediate compounds of Formulae (7) to (12) (or to (13)) to compounds of Formula (1) in Scheme 2.

Compounds of Formula (1), where Z is COH, may be converted to compounds of Formula (2) as illustrated in 25 Scheme 16. Treatment with various alkylating agents R¹⁴X (where R¹⁴ is defined above and X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in the presence or absence of a base in an inert solvent to afford structures (2). It will be recognized by one skilled in the art that the methods used in Scheme 16 30 may also be used to prepare compounds of Formula (1) where Z is COR⁷.

For Scheme 16, the terms "base" and "inert solvent" may have the meanings given below. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), 35 alkali metal bis(trialkylsilyl)amides (preferably

sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20°C to 100°C.

EXAMPLES

Analytical data were recorded for the compounds described below using the following general procedures. Proton NMR spectra were recorded on an IBM-Bruker FT-NMR (300 MHz); chemical shifts were recorded in ppm (δ) from an internal tetramethylsilane standard in deuteriochloroform or deuteriodimethylsulfoxide as specified below. Mass spectra (MS) or high resolution mass spectra (HRMS) were recorded on a Finnegan MAT 8230 spectrometer (using chemi-ionization (CI) with NH₃ as the carrier gas or gas chromatography (GC) as specified below) or a Hewlett Packard 5988A model spectrometer. Melting points were recorded on a Buchi Model 510 melting point apparatus and are uncorrected. Boiling points are uncorrected. All pH determinations during workup were made with indicator paper.

Reagents were purchased from commercial sources

- and, where necessary, purified prior to use according to the general procedures outlined by D. Perrin and W.L.F. Armarego, *Purification of Laboratory Chemicals*, 3rd ed., (New York: Pergamon Press, 1988).
- 5 Chromatography was performed on silica gel using the solvent systems indicated below. For mixed solvent systems, the volume ratios are given. Otherwise, parts and percentages are by weight.
- 10 The following examples are provided to describe the invention in further detail. These examples, which set forth the best mode presently contemplated for carrying out the invention, are intended to illustrate and not to limit the invention.
- 15
- EXAMPLE 1**
- Preparation of
- 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-
20 -pyrazolo-[1,3,5]-triazin-4(3H)-one
(Formula 7, where Y is O, R₁ is CH₃, Z is C-CH₃,
Ar is 2,4-dimethylphenyl)
- A. 1-Cyano-1-(2,4-dimethylphenyl)propan-2-one
- 25 Sodium pellets (9.8g, 0.43 mol) were added portionwise to a solution of 2,4-dimethylphenylacetonitrile (48 g, 0.33 mol) in ethyl acetate (150 mL) at ambient temperature. The reaction mixture was heated to reflux temperature and stirred
- 30 for 16 hours. The resulting suspension was cooled to room temperature and filtered. The collected precipitate was washed with copious amounts of ether and then air-dried. The solid was dissolved in water and a 1N HCl solution was added until the pH = 5-6. The
- 35 mixture was extracted with ethyl acetate (3 X 200 mL);

the combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to afford a white solid (45.7g, 74% yield): NMR (CDCl₃, 300 MHz):; CI-MS: 188 (M + H).

5

B. 5-Amino-4-(2,4-dimethylphenyl)-3-methylpyrazole

- A mixture of 1-cyano-1-(2,4-dimethylphenyl)propan-2-one (43.8g, 0.23 mol), hydrazine-hydrate (22 mL, 0.46 mol), glacial acetic acid (45 mL, 0.78 mol) and toluene (500 mL) were stirred at reflux temperature for 18 hours in an apparatus fitted with a Dean-Stark trap. The reaction mixture was cooled to ambient temperature and solvent was removed *in vacuo*. The residue was dissolved in 6N HCl and the resulting solution was extracted with ether three times. A concentrated ammonium hydroxide solution was added to the aqueous layer until pH = 11. The resulting semi-solution was extracted three times with ethyl acetate. The combined organic layers were dried over MgSO₄ and filtered.
- 10 Solvent was removed *in vacuo* to give a pale brown viscous oil (34.6g, 75% yield): NMR (CDCl₃, 300 MHz): 7.10 (s, 1H), 7.05 (d, 2H, J=1), 2.37 (s, 3H), 2.10 (s, 3H); CI-MS: 202 (M + H).

15 20 25 C. 5-Acetamidino-4-(2,4-dimethylphenyl)-3-methylpyrazole, acetic acid salt

- Ethyl acetamide hydrochloride (60g, 0.48 mol) was added quickly to a rapidly stirred mixture of potassium carbonate (69.5g, 0.50 mol), dichloromethane (120 mL) and water (350 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (2 X 120 mL). The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed by simple distillation and the pot residue, a

clear pale yellow liquid, (35.0 g) was used without further purification.

Glacial aetic acid (9.7 mL, 0.17 mol) was added to a stirred mixture of 5-amino-4-(2,4-dimethylphenyl)-3-methylpyrazole (34g, 0.17 mol), ethyl acetamide (22g, 0.25 mol) and acetonitrile (500 mL). The resulting reaction mixture was stirred at room temperature for 3 days; at the end of which time, it was concentrated in vacuo to about one-third of its original volume. The resulting suspension was filtered and the collected solid was washed with copious amounts of ether. The white solid was dried in vacuo (31.4g, 61% yield): NMR (DMSO-d₆, 300 MHz): 7.00 (s, 1H), 6.90 (dd, 2H, J=7, 1), 2.28 (s, 3H), 2.08 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H), 1.81 (s, 3H); CI-MS: 243 (M + H).

D. 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-[1,3,5]-triazin-4(3H)-one

Sodium pellets (23g, 1 mol) were added portionwise to ethanol (500 mL) with vigorous stirring. After all the sodium reacted, 5-acetamidino-4-(2,4-dimethylphenyl)-3-methylpyrazole, acetic acid salt (31.2g, 0.1 mol) and diethyl carbonate (97 mL, 0.8 mol) were added. The resulting reaction mixture was heated to reflux temperature and stirred for 18 hours. The mix was cooled to room temperature and solvent was removed in vacuo. The residue was dissolved in water and a 1N HCl solution was added slowly until pH = 5-6. The aqueous layer was extracted with ethyl acetate three times; the combined organic layers were dried over MgSO₄ and filtered. Solvent was removed in vacuo to give a pale tan solid (26g, 98% yield): NMR (CDCl₃, 300 MHz): 7.15 (s, 1H), 7.09 (s, 2H), 2.45 (s, 3H), 2.39 (s, 3H), 2.30 (s, 3H); CI-MS: 269 (M + H).

EXAMPLE 2

Preparation of

5 5-methyl-3-(2,4,6-trimethylphenyl)[1,5-a]-
[1,2,3]-triazolo-[1,3,5]-triazin-7(6H)-one
(Formula 7, where Y is O, R₁ is CH₃, Z is N,
Ar is 2,4,6-trimethylphenyl)

10 A. 1-Phenylmethyl-4-(2,4,6-trimethylphenyl)-5-
aminotriazole

15 A mixture of 2,4,6-trimethylbenzyl cyanide (1.0g,
6.3 mmol), benzyl azide (0.92g, 6.9 mmol) and potassium
t-butoxide (0.78g, 6.9 mmol) in tetrahydrofuran (10mL)
was stirred at ambient temperature for 2.5 days. The
resulting suspension was diluted with water and
extracted three times with ethyl acetate. The combined
organic layers were dried over MgSO₄ and filtered.

20 Solvent was removed in vacuo to give a brown oil.
Trituration with ether and filtration afforded a yellow
solid (1.12g, 61% yield): NMR (CDCl₃, 300 MHz): 7.60-7.30
(m, 5H), 7.30-7.20 (m, 2H), 5.50 (s, 2H), 3.18 (br s,
2H), 2.30 (s, 3H), 2.10 (s, 6H); CI-MS: 293 (M + H).

25 B. 4-(2,4,6-Trimethylphenyl)-5-aminotriazole

30 Sodium (500 mg, 22 mmol) was added with stirring
to a mixture of liquid ammonia (30 mL) and 1-
phenylmethyl-4-(2,4,6-trimethylphenyl)-5-aminotriazole
(1.1g, 3.8 mmol). The reaction mixture was stirred
until a dark green color persisted. An ammonium
chloride solution (mL) was added and the mixture was
stirred while warming to ambient temperature over 16
hours. The residue was treated with a 1M HCl solution
and filtered. The aqueous layer was basified with a
concentrated ammonium hydroxide solution (pH = 9) and
then extracted with ethyl acetate three times. The

combined organic layers were dried over MgSO₄ and filtered. Solvent was removed in vacuo to give a yellow solid (520 mg), which was homogeneous by thin layer chromatography (ethyl acetate):

5 NMR (CDCl₃, 300 MHz): 6.97 (s, 2H), 3.68-3.50 (br.s, 2H), 2.32 (s, 3H), 2.10 (s, 6H); CI-MS: 203 (M + H).

C. 4-(2,4,6-Trimethylphenyl)-5-acetamidinotriazole, acetic acid salt

10 A mixture of 4-(2,4,6-trimethylphenyl)-5-aminotriazole (400 mg, 1.98 mmol), ethyl acetamide (261 mg, 3 mmol) and glacial acetic acid (0.1 mL, 1.98 mmol) in acetonitrile (6 mL) was stirred at ambient temperature for 4 hours. The resulting suspension was 15 filtered and the collected solid was washed with copious amounts of ether. Drying in vacuo afforded a white solid (490 mg, 82% yield): NMR (DMSO-d₆, 300 MHz): 7.90-7.70 (br s, 0.5H), 7.50-7.20 (br. s, 0.5H), 6.90 (s, 2H), 6.90 (s, 2H), 3.50-3.10 (br s, 3H), 2.30-20 2.20 (br s, 3H), 2.05 (d, 1H, J = 7), 1.96 (s, 6H), 1.87 (s, 6H); CI-MS: 244 (M + H).

D. 5-methyl-3-(2,4,6-trimethylphenyl)[1,5-a]-[1,2,3]-triazolo-[1,3,5]-triazin-7(4H)-one

25 Sodium (368 mg, 16.2 mmol) was added with stirring to ethanol (10 mL) at room temperature. After the sodium had reacted, 4-(2,4,6-trimethylphenyl)-5-acetamido-triazole, acetic acid salt (490 mg, 1.6 mmol) and diethyl carbonate (1.6 mL, 13 mmol) were 30 added. The reaction mixture was stirred at reflux temperature for 5 hours, then cooled to room temperature. The reaction mixture was diluted with water; a 1N HCl solution was added until pH = 5-6 and three extractions with ethyl acetate were performed.

The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a yellow residue. Trituration with ether and filtration afforded a yellow solid (300 mg, 69% yield): NMR (CDCl₃, 300 MHz): 6.98 (s, 2H), 2.55 (s, 3H), 2.35 (s, 3H), 2.10 (s, 6H); CI-MS: 270 (M + H).
5

EXAMPLE 3

Preparation of 4-(di(carbomethoxy)methyl)-
10 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-
1,3,5-triazine
(Formula 1, where R³ is CH(CHCO₂CH₃)₂, R₁ is CH₃, Z is C-CH₃, Ar is 2,4-dimethylphenyl)

15 A. 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolotriazine
A mixture of 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-1,3,5-triazin-4-one (Example 1, 1.38g, 4.5 mmol), N,N-dimethylaniline (1 mL, 8 mmol) and phosphorus oxychloride (10 mL) was stirred at reflux temperature for 48 hours. The excess phosphorus oxychloride was removed *in vacuo*. The residue was poured onto ice-water, stirred briefly and extracted quickly with ethyl acetate three times. The combined organic layers were washed with ice water, then dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a brown oil. Flash column chromatography (ethyl acetate:hexanes::1:4) gave one fraction (R_f = 0.5). Solvent was removed *in vacuo* to afford a yellow oil (1.0g, 68% yield): NMR (CDCl₃, 300 MHz): 7.55 (d, 1H, J = 1), 7.38 (dd, 1H, J = 7, 1), 7.30 (d, 1H, J = 7), 2.68 (s, 3H), 2.45 (s, 3H); CI-MS: 327 (M + H).
20
25
30

B. 4-(di(carbomethoxy)methyl)-2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-1,3,5-triazine
Sodium hydride (60% in oil, 80 mg, 2 mmol) was
5 washed with hexanes twice, decanted after each washing
and taken up in anhydrous tetrahydrofuran (THF, 1 mL).
A solution of diethyl malonate (0.32g, 2 mmol) in THF
(2 mL) was added dropwise over 5 min, during which time
vigorous gas evolution ensued. A solution of 4-chloro-
10 2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-
pyrazolotriazine (0.5g, 1.75 mmol) in THF (2 mL)
was added and the reaction mixture was then stirred
under a nitrogen atmosphere for 48 hours. The
resulting suspension was poured onto water and
15 extracted three times with ethyl acetate. The combined
organic layers were washed once with brine, dried over
 MgSO_4 and filtered. Solvent was removed in vacuo to
give a brown oil. Column chromatography (ethyl
acetate:hexanes::1:9) afforded, after removal of
20 solvent in vacuo, a pale yellow solid ($R_f = 0.2$, 250
mg, 35% yield): mp 50-52°C; NMR (CDCl_3 , 300 MHz): 12.35
(br.s, 1H, 7.15-7.00 (m, 3H), 4.40 (q, 2H, $J = 7$), 4.30
(q, 2H, $J = 7$), 2.4, 2.35, 2.3, 2.2, 2.1 (5 s, 12H),
1.4 (t, 3H, $J = 7$), 1.35-1.25 (m, 3H); CI-HRMS: Calcd:
25 411.2032, Found: 411.2023.

EXAMPLE 6

Preparation of 4-(1,3-dimethoxy-2-propylamino)-
30 2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-
1,3,5-triazine
(Formula 1, where R^3 is $\text{NHCH}(\text{CH}_2\text{OCH}_3)_2$, R_1 is CH_3 , Z is
 $\text{C}-\text{CH}_3$, Ar is 2,4-dichlorophenyl)

A. 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolotriazine

A mixture of 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-1,3,5-triazin-4-one (Example 1, 1.38g, 4.5 mmol), N,N-dimethylaniline (1 mL, 8 mmol) and phosphorus oxychloride (10 mL) was stirred at reflux temperature for 48 hours. The excess phosphorus oxychloride was removed in vacuo. The residue was poured onto ice-water, stirred briefly and extracted quickly with ethyl acetate three times. The combined organic layers were washed with ice water, then dried over MgSO₄ and filtered. Solvent was removed in vacuo to give a brown oil. Flash column chromatography (ethyl acetate:hexanes::1:4) gave one fraction (*R*_f = 0.5). Solvent was removed in vacuo to afford a yellow oil (1.0g, 68% yield): NMR (CDCl₃, 300 MHz): 7.55 (d, 1H, J = 1), 7.38 (dd, 1H, J = 7, 1), 7.30 (d, 1H, J = 7), 2.68 (s, 3H), 2.45 (s, 3H); CI-MS: 327 (M + H).

20

B. 4-(1,3-dimethoxy-2-propylamino)-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-1,3,5-triazine

A mixture of 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-1,3,5-triazine (Part A, 570 mg, 1.74 mmol), 1,3-dimethoxypropyl-2-aminopropane (25mg, 2.08 mmol) and ethanol (10 mL) was stirred at ambient temperature for 18 hours. The reaction mixture was poured onto water (25 mL) and extracted three times with ethyl acetate. The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed in vacuo. Column chromatography (CH₂Cl₂:CH₃OH::50:1) afforded one fraction. Removal of solvent in vacuo gave a solid (250 mg, 35% yield): mp 118-120°C; NMR (CDCl₃, 300 MHz): 7.50 (s, 1H), 7.28 (dd, 2H, J = 8, 1),

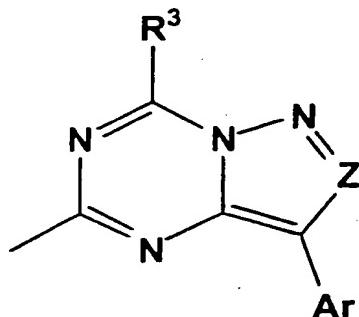
6.75 (d, 1H, J = 8), 4.70-4.58 (m, 1H), 3.70-3.55 (m, 4H), 3.43 (s, 6H), 2.50 (s, 3H), 2.35 (s, 3H); CI-HRMS: Calcd: 409.1072, Found: 409.1085; Analysis Calcd. for C₁₈H₂₁Cl₂N₅O₂: C, 52.69, H, 5.17, N, 17.07, Cl, 17.28;
5 Found: C, 52.82, H, 5.06, N, 16.77, Cl, 17.50.

Using the above procedures and modifications known to one skilled in the art of organic synthesis, the following additional examples of Tables 1-4 may be
10 prepared.

The examples delineated in TABLE 1 may be prepared by the methods outlined in Examples 1, 2, 3 or 6. Commonly used abbreviations are: Ph is phenyl, Pr is
15 propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example.

TABLE 1

20



	<u>Ex.</u>	<u>Z</u>	<u>R₃</u>	<u>Ar</u>	<u>mp (°C)</u>
25	6 ^a	C-Me	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	118-120
	391 ^{bz}	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph	oil

	395 ^{bu}	C-Me	NEt ₂	2-Me-4,6-(MeO) ₂ Ph	114					
	396 ^{bv}	C-Me	NH-3-pentyl	2-Me-4,6-(MeO) ₂ Ph						
					145-146					
5										
NOTES FOR TABLE 1:										
a) Analysis Calcd: C, 52.69, H, 5.17, N, 17.07, Cl, 17.28; Found: C, 52.82, H, 5.06, N, 16.77, Cl, 17.50.										
10	bu)	Analysis Calcd: C: 65.90, H: 7.72, N, 18.27; Found: C: 65.77, H: 7.62, N: 18.26.								
	bv)	Analysis Calcd: C: 65.02, H: 7.38, N, 18.96; Found: C: 65.01, H: 7.43, N: 18.68.								
	bz)	CI-HRMS: Calcd: 430.2454; Found: 430.2468(M + H);								
15										

EXAMPLE 431

Preparation of 2,4,7-dimethyl-8-(4-methoxy-2-methylphenyl)[1,5-a]-pyrazolo-1,3,5-triazine
 20 (Formula 1, where R³ is CH₃, R₁ is CH₃, Z is C-CH₃, Ar is 2,4-dimethylphenyl)

5-Acetamidino-4-(4-methoxy-2-methylphenyl)-3-methylpyrazole, acetic acid salt (602 mg, 2 mmol) was mixed with a saturated NaHCO₃ solution (10 mL). The aqueous mixture was extracted with EtOAc three times. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue was taken up in toluene (10 mL) and trimethyl orthoacetate (0.36 g, 3 mmol) was added to the suspension. The reaction mixture was heated to reflux temperature under a nitrogen atmosphere and stirred for 16 hours. After being cooled to ambient temperature, the reaction

mixture was concentrated in vacuo to give an oily solid. Column chromatography ($\text{CHCl}_3:\text{MeOH}::9:1$) afforded, after removal of solvent in vacuo, a yellow viscous oil ($R_f = 0.6$, 210 mg, 37% yield): NMR (CDCl_3 , 5 300 MHz): 7.15 (d, 1H, $J = 8$), 6.9 (d, 1H, $J = 1$), 6.85 (dd, 1H, $J = 8,1$), 3.85 (s, 3H), 2.95 (s, 3H), 2.65 (s, 3H), 2.4 (s, 3H), 2.15 (s, 3H); CI-HRMS: Calcd: 283.1559, Found: 283.1554 ($M + H$).

10

EXAMPLE 432

15 7-hydroxy-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine
(Formula 1 where A is CH, R1 is Me, R3 is OH, Z is C-Me, Ar is 2-chloro-4-methylphenyl)

20 5-Amino-4-(2-chloro-4-methylphenyl)-3-methylpyrazole (1.86 g, 8.4 mmol) was dissolved in glacial acetic acid (30 mL) with stirring. Ethyl acetoacetate (1.18 mL, 9.2 mmol) was then added dropwise to the resulting solution. The reaction mixture was then heated to reflux temperature and 25 stirred for 16 hours, then cooled to room temperature. Ether (100 mL) was added and the resulting precipitate was collected by filtration. Drying in vacuo afforded a white solid (1.0 g, 42% yield): NMR (CDCl_3 , 300Hz): 8.70 (br.s 1H), 7.29 (s, 1H), 7.21-7.09 (m, 2H), 5.62 (s, 1H), 2.35 (s, 6H), 2.29 (s, 3H); CI-MS: 288 ($M+H$).

EXAMPLE 433

35 7-chloro-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine

(Formula 1 where A is CH, R1 is Me, R3 is Cl,
Z is C-Me, Ar is 2-chloro-4-methylphenyl)

A mixture of 7-hydroxy-5-methyl-3-(2-chloro-4-methylphenyl)-pyrazolo[1,5-a]pyrimidine (1.0 g, 3.5 mmol), phosphorus oxychloride (2.7 g, 1.64 mL, 17.4 mmol), N,N-diethylaniline (0.63 g, 0.7 mL, 4.2 mmol) and toluene (20 mL) was stirred at reflux temperature for 3 hours, then it was cooled to ambient temperature.

10 The volatiles were removed in vacuo. Flash chromatography (EtOAc:hexane::1:2) on the residue gave 7-chloro-5-methyl-3-(2-chloro-4-methylphenyl)-pyrazolo[1,5-a]pyrimidine (900 mg, 84% yield) as a yellow oil: NMR (CDCl_3 , 300Hz): 7.35 (s, 1H), 7.28-15 7.26 (m, 1H), 71.6 (d, 1H, $J = 7$), 6.80 (s, 1H), 2.55 (s, 3H), 2.45 (s, 3H), 2.40 (s, 3H); CI- MS: 306 ($M+H$) .

EXAMPLE 434

20 7-(pentyl-3-amino)-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine
(Formula 1 where A is CH, R1 is Me, R3 is pentyl-3-amino, Z is C-Me, Ar is 2-chloro-4-methylphenyl)

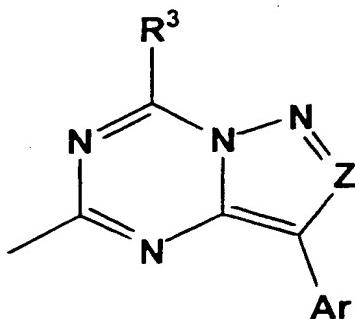
25 A solution of 3-pentylamine (394mg, 6.5 mmol) and 7-chloro-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine (200 mg, 0.65 mmol) in dimethylsulfoxide (DMSO, 10 mL) was stirred at 150°C for 2 hours; then it was cooled to ambient 30 temperature. The reaction mixture was then poured onto water (100 mL) and mixed. Three extractions with dichloromethane, washing the combined organic layers with brine, drying over MgSO_4 , filtration and removal of solvent in vacuo produced a yellow solid. Flash 35 chromatography (EtOAc:hexanes::1:4) afforded a white

solid (140 mg, 60% yield): mp 139-141°C; NMR (CDCl_3 , 300Hz): 7.32 (s, 1H), 7.27 (d, 1H, $J = 8$), 7.12 (d, 1H, $J = 7$), 6.02 (d, 1H, $J = 9$), 5.78 (s, 1H), 3.50-3.39 (m, 1H), 2.45 (s, 3H), 2.36 (s, 6H), 1.82-1.60 (m, 4H), 5 1.01 (t, 6H, $J = 8$); Analysis Calcd for $\text{C}_{20}\text{H}_{25}\text{ClN}_4$: C, 67.31, H, 7.06, N, 15.70, Cl: 9.93; Found: C, 67.32, H, 6.95, N, 15.50, Cl, 9.93.

10 The examples delineated in Table 7 may be prepared by the methods outlined in Examples 1, 2, 3 or 6. Commonly used abbreviations are: Ph is phenyl, Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example.

15

Table 7



	<u>Ex.</u>	<u>Z</u>	<u>R_3</u>	<u>Ar</u>	<u>mp (°C)</u>
20	1200 ^a	C-Me	2-ethylpiperidyl	2-Me-4-OMePh	58-
		59.5			
25	1201 ^b	C-Me	cyclobutylamino	2-Me-4-OMePh	94.5-
	96				
	1202 ^c	C-Me	$\text{N}(\text{Me})\text{CH}_2\text{CH}=\text{CH}_2$	2-Me-4-OMePh	oil
	1203 ^d	C-Me	$\text{N}(\text{CH}_2\text{CH}=\text{CH}_2)_2$	2-Me-4-OMePh	oil

	1204	C-Me	N(Et)CH ₂ C-Pr	2-Me-4-OMePh	
	1205 ^e	C-Me	NHCH ₂ -2-tetrahydrofuryl	2-Me-4-OMePh	
			amorphous		
5	1206 ^{ay}	C-Me	N(Pr)CH ₂ C-Pr	2-Me-4-OMePh	oil
	1207 ^{az}	C-Me	N(Me)Pr	2-Me-4-OMePh	oil
	1208 ^f	C-Me	N(Me)Et	2-Me-4-OMePh	oil
	1209 ^g	C-Me	N(Me)Bu	2-Me-4-OMePh	oil
10	1210 ^h	C-Me	N(Me)propargyl	2-Me-4-OMePh	oil
	1211 ⁱ	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Me-4-OMePh	oil
	1212 ^j	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Me-4-OMePh	oil
	1213 ^k	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Me-4-OMePh	oil
	1214	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Me-4-OMePh	
15	1215	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Me-4-OMePh	
	1216	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Me-4-OMePh	
	1217 ^m	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Me-4-OMePh	oil
	1218	C-Me	NHCH(c-Pr) ₂	2-Me-4-OMePh	
	1219 ⁿ	C-Me	NH-2-hexyl	2-Me-4-OMePh	oil
20	1220 ^o	C-Me	NH-2-propyl	2-Me-4-OMePh	oil
	1221 ^p	C-Me	NHCH ₂ -2-tetrahydrofuryl	2-Me-4-OMePh	
			amorphous		
	1222 ^q	C-Me	NET(cyclohexyl)	2-Me-4-OMePh	oil
	1223	C-Me	2-ethylpiperidyl	2,5-Me ₂ -4-OMePh	
25	1224	C-Me	cyclobutylamino	2,5-Me ₂ -4-OMePh	
	1225	C-Me	N(Me)CH ₂ CH=CH ₂	2,5-Me ₂ -4-OMePh	
	1226	C-Me	N(Et)CH ₂ C-Pr	2,5-Me ₂ -4-OMePh	
	1227	C-Me	N(Pr)CH ₂ C-Pr	2,5-Me ₂ -4-OMePh	
	1228	C-Me	N(Me)Pr	2,5-Me ₂ -4-OMePh	
30	1229	C-Me	N(Me)Et	2,5-Me ₂ -4-OMePh	

	1230	C-Me	N(Me)Bu	2,5-Me ₂ -4-OMePh
	1231	C-Me	N(Me)propargyl	2,5-Me ₂ -4-OMePh
	1232	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2,5-Me ₂ -4-OMePh
	1233	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2,5-Me ₂ -4-OMePh
5	1234	C-Me	N(CH ₂ CH ₂ OMe)Me	2,5-Me ₂ -4-OMePh
	1235	C-Me	N(CH ₂ CH ₂ OMe)Et	2,5-Me ₂ -4-OMePh
	1236	C-Me	N(CH ₂ CH ₂ OMe)Pr	2,5-Me ₂ -4-OMePh
	1237	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2,5-Me ₂ -4-OMePh
	1238	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2,5-Me ₂ -4-OMePh
10	1239	C-Me	NHCH(c-Pr) ₂	2,5-Me ₂ -4-OMePh
	1240	C-Me	2-ethylpiperidyl	2,4-(OMe) ₂ Ph
	1241	C-Me	cyclobutylamino	2,4-(OMe) ₂ Ph
	1245	C-Me	N(Me)CH ₂ CH=CH ₂	2,4-(OMe) ₂ Ph
	1255 ^x	C-Me	N(CH ₂ CH=CH ₂) ₂	2,4-(OMe) ₂ Ph 64.8-
15	65.6			
	1256	C-Me	N(Et)CH ₂ c-Pr	2,4-(OMe) ₂ Ph
	1257	C-Me	N(Pr)CH ₂ c-Pr	2,4-(OMe) ₂ Ph
	1258	C-Me	N(Me)Pr	2,4-(OMe) ₂ Ph
	1259	C-Me	N(Me)Et	2,4-(OMe) ₂ Ph
20	1260	C-Me	N(Me)Bu	2,4-(OMe) ₂ Ph
	1261	C-Me	N(Me)propargyl	2,4-(OMe) ₂ Ph
	1262	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2,4-(OMe) ₂ Ph
	1263	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2,4-(OMe) ₂ Ph
	1264	C-Me	N(CH ₂ CH ₂ OMe)Me	2,4-(OMe) ₂ Ph
25	1265	C-Me	N(CH ₂ CH ₂ OMe)Et	2,4-(OMe) ₂ Ph
	1266	C-Me	N(CH ₂ CH ₂ OMe)Pr	2,4-(OMe) ₂ Ph
	1267	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2,4-(OMe) ₂ Ph
	1268 ^s	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2,4-(OMe) ₂ Ph 137.8-
	138.3			
30	1269	C-Me	NHCH(c-Pr) ₂	2,4-(OMe) ₂ Ph

	1270^t	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,4-(OMe) ₂ Ph	oil
	1271^u	C-Me	NHCH(Et) ₂	2,4-(OMe) ₂ Ph	128-
	129.4				
	1272	C-Me	N(Et) ₂	2,4-(OMe) ₂ Ph	
5	1273^v	C-Me	N(Pr) ₂	2,4-(OMe) ₂ Ph	
	1274	C-Me	2-ethylpiperidyl	2,4-(OMe) ₂ -5-MePh	
	1275	C-Me	cyclobutylamino	2,4-(OMe) ₂ -5-MePh	
	1276	C-Me	N(Me)CH ₂ CH=CH ₂	2,4-(OMe) ₂ -5-MePh	
	1277	C-Me	N(Et)CH ₂ C-Pr	2,4-(OMe) ₂ -5-MePh	
10	1278	C-Me	N(Pr)CH ₂ C-Pr	2,4-(OMe) ₂ -5-MePh	
	1279	C-Me	N(Me)Pr	2,4-(OMe) ₂ -5-MePh	
	1280	C-Me	N(Me)Et	2,4-(OMe) ₂ -5-MePh	
	1281	C-Me	N(Me)Bu	2,4-(OMe) ₂ -5-MePh	
	1282	C-Me	N(Me)propargyl	2,4-(OMe) ₂ -5-MePh	
15	1283	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃) ₂ ,4-(OMe) ₂ -5-MePh		
	1284	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂ 2,4-(OMe) ₂ -5-MePh		
	1285	C-Me	N(CH ₂ CH ₂ OMe)Me	2,4-(OMe) ₂ -5-MePh	
	1286	C-Me	N(CH ₂ CH ₂ OMe)Et	2,4-(OMe) ₂ -5-MePh	
	1287	C-Me	N(CH ₂ CH ₂ OMe)Pr	2,4-(OMe) ₂ -5-MePh	
20	1288	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2,4-(OMe) ₂ -5-MePh	
	1289	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2,4-(OMe) ₂ -5-MePh	
	1290	C-Me	NHCH(c-Pr) ₂	2,4-(OMe) ₂ -5-MePh	
	1291	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,4-(OMe) ₂ -5-MePh	
	1292	C-Me	NHCH(Et) ₂	2,4-(OMe) ₂ -5-MePh	
25	1293	C-Me	N(Et) ₂	2,4-(OMe) ₂ -5-MePh	
	1294	C-Me	2-ethylpiperidyl	2,4-(OMe) ₂ -5-ClPh	
	1295	C-Me	cyclobutylamino	2,4-(OMe) ₂ -5-ClPh	
	1296	C-Me	N(Me)CH ₂ CH=CH ₂	2,4-(OMe) ₂ -5-ClPh	
	1297	C-Me	N(Et)CH ₂ C-Pr	2,4-(OMe) ₂ -5-ClPh	
30	1298	C-Me	N(Pr)CH ₂ C-Pr	2,4-(OMe) ₂ -5-ClPh	

1299	C-Me	N(Me)Pr	2,4-(OMe) ₂ -5-ClPh	
1300	C-Me	N(Me)Et	2,4-(OMe) ₂ -5-ClPh	
1301	C-Me	N(Me)Bu	2,4-(OMe) ₂ -5-ClPh	
1302	C-Me	N(Me)propargyl	2,4-(OMe) ₂ -5-ClPh	
5	1303	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃) ₂ ,4-(OMe) ₂ -5-ClPh	
	1304	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂ 2,4-(OMe) ₂ -5-ClPh	
	1305	C-Me	N(CH ₂ CH ₂ OMe)Me	2,4-(OMe) ₂ -5-ClPh
	1306	C-Me	N(CH ₂ CH ₂ OMe)Et	2,4-(OMe) ₂ -5-ClPh
	1307	C-Me	N(CH ₂ CH ₂ OMe)Pr	2,4-(OMe) ₂ -5-ClPh
10	1308	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2,4-(OMe) ₂ -5-ClPh
	1309	C-Me	NH(CH(CH ₃)CH ₂ CH ₃) ₂	2,4-(OMe) ₂ -5-ClPh
	1310	C-Me	NHCH(c-Pr) ₂	2,4-(OMe) ₂ -5-ClPh
	1311	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,4-(OMe) ₂ -5-ClPh
	1312	C-Me	NHCH(Et) ₂	2,4-(OMe) ₂ -5-ClPh
15	1313	C-Me	N(Et) ₂	2,4-(OMe) ₂ -5-ClPh
	1314 ^y	C-Me	2-ethylpiperidyl	2-Me-4,6-(OMe) ₂ Ph
				145-149
	1315 ^z	C-Me	cyclobutylamino	2-Me-4,6-(OMe) ₂ Ph
				131-133
20	1316 ^{aa}	C-Me	N(Me)CH ₂ CH=CH ₂	2-Me-4,6-(OMe) ₂ Ph oil
	1317	C-Me	N(Et)CH ₂ c-Pr	2-Me-4,6-(OMe) ₂ Ph
	1318 ^{ab}	C-Me	N(Pr)CH ₂ c-Pr	2-Me-4,6-(OMe) ₂ Ph oil
25	1319 ^{ac}	C-Me	N(Me)Pr	2-Me-4,6-(OMe) ₂ Ph oil
	1320 ^{ad}	C-Me	N(Me)Et	2-Me-4,6-(OMe) ₂ Ph oil
	1321 ^{ae}	C-Me	N(Me)Bu	2-Me-4,6-(OMe) ₂ Ph oil

			N(Me)propargyl	2-Me-4, 6-(OMe) ₂ Ph	
1322	C-Me		NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Me-4, 6-(OMe) ₂ Ph	
1323	C-Me		N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Me-4, 6-(OMe) ₂ Ph	
1324	C-Me		N(CH ₂ CH ₂ OMe)Me	2-Me-4, 6-(OMe) ₂ Ph	
1325	C-Me		N(CH ₂ CH ₂ OMe)Et	2-Me-4, 6-(OMe) ₂ Ph	oil
5	1326 ^{af}	C-Me			
1327	C-Me		N(CH ₂ CH ₂ OMe)Pr	2-Me-4, 6-(OMe) ₂ Ph	
1328 ^{ag}	C-Me		N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Me-4, 6-(OMe) ₂ Ph	oil
10	1329 ^{ax}	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Me-4, 6-(OMe) ₂ Ph	
					107-110
1330	C-Me		NHCH(c-Pr) ₂	2-Me-4, 6-(OMe) ₂ Ph	
1331 ^w	C-Me		N(CH ₂ CH ₂ OMe) ₂	2-Me-4, 6-(OMe) ₂ Ph	
1332	C-Me		NHCH(Et) ₂	2-Me-4, 6-(OMe) ₂ Ph	
15	1333	C-Me	N(Et) ₂	2-Me-4, 6-(OMe) ₂ Ph	
1334 ^x	C-Me		NET(Bu)	2-Me-4, 6-(OMe) ₂ Ph	oil
1335	C-Me		2-ethylpiperidyl	2-Cl-4, 6-(OMe) ₂ Ph	
1336	C-Me		cyclobutylamino	2-Cl-4, 6-(OMe) ₂ Ph	
1337	C-Me		N(Me)CH ₂ CH=CH ₂	2-Cl-4, 6-(OMe) ₂ Ph	
20	1338	C-Me	N(Et)CH ₂ C-Pr	2-Cl-4, 6-(OMe) ₂ Ph	
1339	C-Me		N(Pr)CH ₂ C-Pr	2-Cl-4, 6-(OMe) ₂ Ph	
1340	C-Me		N(Me)Pr	2-Cl-4, 6-(OMe) ₂ Ph	
1341	C-Me		N(Me)Et	2-Cl-4, 6-(OMe) ₂ Ph	
1342	C-Me		N(Me)Bu	2-Cl-4, 6-(OMe) ₂ Ph	
25	1343	C-Me	N(Me)propargyl	2-Cl-4, 6-(OMe) ₂ Ph	
1344	C-Me		NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4, 6-(OMe) ₂ Ph	
1345	C-Me		N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4, 6-(OMe) ₂ Ph	
1346	C-Me		N(CH ₂ CH ₂ OMe)Me	2-Cl-4, 6-(OMe) ₂ Ph	
1347	C-Me		N(CH ₂ CH ₂ OMe)Et	2-Cl-4, 6-(OMe) ₂ Ph	
30	1348	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4, 6-(OMe) ₂ Ph	

	1349	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4,6-(OMe) ₂ Ph
	1350	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4,6-(OMe) ₂ Ph
	1351	C-Me	NHCH(c-Pr) ₂	2-Cl-4,6-(OMe) ₂ Ph
	1352	C-Me	NHCH(Et) ₂	2-Cl-4,6-(OMe) ₂ Ph
5	1353	C-Me	N(Et) ₂	2-Cl-4,6-(OMe) ₂ Ph
	1354	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-Ph
	1355	C-Me	cyclobutylamino	2-Cl-4-OMe-Ph
	1356	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4-OMe-Ph
	1357	C-Me	N(Et)CH ₂ C-Pr	2-Cl-4-OMe-Ph
10	1358	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-4-OMe-Ph
	1359	C-Me	N(Me)Pr	2-Cl-4-OMe-Ph
	1360	C-Me	N(Me)Et	2-Cl-4-OMe-Ph
	1361	C-Me	N(Me)Bu	2-Cl-4-OMe-Ph
	1362	C-Me	N(Me)propargyl	2-Cl-4-OMe-Ph
15	1363	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4-OMe-Ph
	1364	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4-OMe-Ph
	1365	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4-OMe-Ph
	1366	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4-OMe-Ph
	1367	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4-OMe-Ph
20	1368	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4-OMe-Ph
	1369	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4-OMe-Ph
	1370	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-Ph
	1371	C-Me	2-ethylpiperidyl	2-Me-4,5-(OMe) ₂ Ph
	1372	C-Me	cyclobutylamino	2-Me-4,5-(OMe) ₂ Ph
25	1373	C-Me	N(Me)CH ₂ CH=CH ₂	2-Me-4,5-(OMe) ₂ Ph
	1374	C-Me	N(Et)CH ₂ C-Pr	2-Me-4,5-(OMe) ₂ Ph
	1375	C-Me	N(Pr)CH ₂ C-Pr	2-Me-4,5-(OMe) ₂ Ph
	1376	C-Me	N(Me)Pr	2-Me-4,5-(OMe) ₂ Ph
	1377	C-Me	N(Me)Et	2-Me-4,5-(OMe) ₂ Ph
30	1378	C-Me	N(Me)Bu	2-Me-4,5-(OMe) ₂ Ph
	1379	C-Me	N(Me)propargyl	2-Me-4,5-(OMe) ₂ Ph

	1380	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)2-Me-4,5-(OMe) ₂ Ph	
	1381	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂ 2-Me-4,5-(OMe) ₂ Ph	
	1382	C-Me	N(CH ₂ CH ₂ OMe)Me 2-Me-4,5-(OMe) ₂ Ph	
	1383	C-Me	N(CH ₂ CH ₂ OMe)Et 2-Me-4,5-(OMe) ₂ Ph	
5	1384	C-Me	N(CH ₂ CH ₂ OMe)Pr 2-Me-4,5-(OMe) ₂ Ph	
	1385	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr 2-Me-4,5-(OMe) ₂ Ph	
	1386	C-Me	NH(CH(CH ₃)CH ₂ CH ₃) 2-Me-4,5-(OMe) ₂ Ph	
	1387	C-Me	NHCH(c-Pr) ₂ 2-Me-4,5-(OMe) ₂ Ph	
	1388	C-Me	N(CH ₂ CH ₂ OMe) ₂ 2-Me-4,5-(OMe) ₂ Ph	
10	1389	C-Me	NHCH(Et) ₂ 2-Me-4,5-(OMe) ₂ Ph	
	1390	C-Me	N(Et) ₂ 2-Me-4,5-(OMe) ₂ Ph	
	1391	C-Me	NEt(Bu) 2-Me-4,5-(OMe) ₂ Ph	
	1392	C-Me	2-ethylpiperidyl 2-Cl-4,5-(OMe) ₂ Ph	
	1393 ^{ab}	C-Me	cyclobutylamino 2-Cl-4,5-(OMe) ₂ Ph	
15				121-122
	1394 ^{ai}	C-Me	N(Me)CH ₂ CH=CH ₂ 2-Cl-4,5-(OMe) ₂ Ph	
				122-126
	1395	C-Me	N(Et)CH ₂ C-Pr 2-Cl-4,5-(OMe) ₂ Ph	
	1396 ^{aj}	C-Me	N(Pr)CH ₂ C-Pr 2-Cl-4,5-(OMe) ₂ Ph oil	
20				
	1397 ^{ak}	C-Me	N(Me)Pr 2-Cl-4,5-(OMe) ₂ Ph	115-117
	1398 ^{al}	C-Me	N(Me)Et 2-Cl-4,5-(OMe) ₂ Ph	115-119
25	1399 ^{am}	C-Me	N(Me)Bu 2-Cl-4,5-(OMe) ₂ Ph oil	
	1400	C-Me	N(Me)propargyl 2-Cl-4,5-(OMe) ₂ Ph	
	1401	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)2-Cl-4,5-(OMe) ₂ Ph	
	1402	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂ 2-Cl-4,5-(OMe) ₂ Ph	
30	1403	C-Me	N(CH ₂ CH ₂ OMe)Me 2-Cl-4,5-(OMe) ₂ Ph	

	1404 ^{an}	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4,5-(OMe) ₂ Ph	oil
	1405	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4,5-(OMe) ₂ Ph	
	1406 ^{ao}	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4,5-(OMe) ₂ Ph	oil
5					
	1407	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4,5-(OMe) ₂ Ph	
	1408	C-Me	NHCH(C-Pr) ₂	2-Cl-4,5-(OMe) ₂ Ph	
	1409 ^{ap}	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(OMe) ₂ Ph	oil
10	1410 ^{aq}	C-Me	NHCH(Et) ₂	2-Cl-4,5-(OMe) ₂ Ph	
					104-106
	1411 ^{ar}	C-Me	N(Et) ₂	2-Cl-4,5-(OMe) ₂ Ph	oil
	1412 ^{as}	C-Me	NEt(Bu)	2-Cl-4,5-(OMe) ₂ Ph	oil
	1413	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-5-MePh	
15	1414	C-Me	cyclobutylamino	2-Cl-4-OMe-5-MePh	
	1415	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4-OMe-5-MePh	
	1416	C-Me	N(Et)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh	
	1417	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh	
	1418	C-Me	N(Me)Pr	2-Cl-4-OMe-5-MePh	
20	1419	C-Me	N(Me)Et	2-Cl-4-OMe-5-MePh	
	1420	C-Me	N(Me)Bu	2-Cl-4-OMe-5-MePh	
	1421	C-Me	N(Me)propargyl	2-Cl-4-OMe-5-MePh	
	1422	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4-OMe-5-MePh	
	1423	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4-OMe-5-MePh	
25	1424	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4-OMe-5-MePh	
	1425	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4-OMe-5-MePh	
	1426	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4-OMe-5-MePh	
	1427	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh	
	1428	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4-OMe-5-MePh	
30	1429	C-Me	NHCH(C-Pr) ₂	2-Cl-4-OMe-5-MePh	
	1430	C-Me	NHCH(Et) ₂	2-Cl-4-OMe-5-MePh	

	1431	C-Me	N(Et) ₂	2-Cl-4-OMe-5-MePh
	1432	C-Me	NEt(Bu)	2-Cl-4-OMe-5-MePh
	1433	C-Me	2-ethylpiperidyl	2-Cl-6-OMe-4-MePh
	1434	C-Me	cyclobutylamino	2-Cl-6-OMe-4-MePh
5	1435	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-6-OMe-4-MePh
	1436	C-Me	N(Et)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1437	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1438	C-Me	N(Me)Pr	2-Cl-6-OMe-4-MePh
	1439	C-Me	N(Me)Et	2-Cl-6-OMe-4-MePh
10	1440	C-Me	N(Me)Bu	2-Cl-6-OMe-4-MePh
	1441	C-Me	N(Me)propargyl	2-Cl-6-OMe-4-MePh
	1442	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-6-OMe-4-MePh
	1443	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-6-OMe-4-MePh
	1444	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-6-OMe-4-MePh
15	1445	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-6-OMe-4-MePh
	1446	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-6-OMe-4-MePh
	1447	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1448	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-6-OMe-4-MePh
	1449	C-Me	NHCH(c-Pr) ₂	2-Cl-6-OMe-4-MePh
20	1450	C-Me	NHCH(Et) ₂	2-Cl-6-OMe-4-MePh
	1451	C-Me	N(Et) ₂	2-Cl-6-OMe-4-MePh
	1452	C-Me	NEt(Bu)	2-Cl-6-OMe-4-MePh
	1453	C-Me	2-ethylpiperidyl	2,6-Me ₂ -4-OMePh
	1454	C-Me	cyclobutylamino	2,6-Me ₂ -4-OMePh
25	1455	C-Me	N(Me)CH ₂ CH=CH ₂	2,6-Me ₂ -4-OMePh
	1456	C-Me	N(Et)CH ₂ C-Pr	2,6-Me ₂ -4-OMePh
	1457	C-Me	N(Pr)CH ₂ C-Pr	2,6-Me ₂ -4-OMePh
	1458	C-Me	N(Me)Pr	2,6-Me ₂ -4-OMePh
	1459	C-Me	N(Me)Et	2,6-Me ₂ -4-OMePh
30	1460	C-Me	N(Me)Bu	2,6-Me ₂ -4-OMePh
	1461	C-Me	N(Me)propargyl	2,6-Me ₂ -4-OMePh

	1462	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2,6-Me ₂ -4-OMePh	
	1463	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2,6-Me ₂ -4-OMePh	
	1464	C-Me	N (CH ₂ CH ₂ OMe) Me	2,6-Me ₂ -4-OMePh	
	1465	C-Me	N (CH ₂ CH ₂ OMe) Et	2,6-Me ₂ -4-OMePh	
5	1466	C-Me	N (CH ₂ CH ₂ OMe) Pr	2,6-Me ₂ -4-OMePh	
	1467	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2,6-Me ₂ -4-OMePh	
	1468	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2,6-Me ₂ -4-OMePh	
	1469	C-Me	NHCH (c-Pr) ₂	2,6-Me ₂ -4-OMePh	
	1470	C-Me	NHCH (Et) ₂	2,6-Me ₂ -4-OMePh	
10	1471	C-Me	N (Et) ₂	2,6-Me ₂ -4-OMePh	
	1472	C-Me	NEt (Bu)	2,6-Me ₂ -4-OMePh	
	1473	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-5-FPh	
	1474	C-Me	cyclobutylamino	2-Cl-4-OMe-5-FPh	
	1475 ^{be}	C-Me	N (Me) CH ₂ CH=CH ₂	2-Cl-4-OMe-5-FPh	oil
15	1476	C-Me	N (Et) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
	1478	C-Me	N (Pr) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
	1479 ^{bb}	C-Me	N (Me) Pr	2-Cl-4-OMe-5-FPh	oil
20	1480 ^{bc}	C-Me	N (Me) Et	2-Cl-4-OMe-5-FPh	oil
	1481	C-Me	N (Me) Bu	2-Cl-4-OMe-5-FPh	
	1482	C-Me	N (Me) propargyl	2-Cl-4-OMe-5-FPh	
	1483	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2-Cl-4-OMe-5-FPh	
25	1484	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2-Cl-4-OMe-5-FPh	
	1485	C-Me	N (CH ₂ CH ₂ OMe) Me	2-Cl-4-OMe-5-FPh	
	1486	C-Me	N (CH ₂ CH ₂ OMe) Et	2-Cl-4-OMe-5-FPh	
	1487	C-Me	N (CH ₂ CH ₂ OMe) Pr	2-Cl-4-OMe-5-FPh	
	1488	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
30	1489 ^{bd}	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2-Cl-4-OMe-5-FPh	
					solid

	1490	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-5-FPh	
	1491 ^{be}	C-Me	NHCH(Et) ₂	2-Cl-4-OMe-5-FPh	oil
	1492 ^{bf}	C-Me	N(Et) ₂	2-Cl-4-OMe-5-FPh	
5					96-98
	1493 ^{bg}	C-Me	NEt(Bu)	2-Cl-4-OMe-5-FPh	oil
	1494	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-6-MePh	
	1495	C-Me	cyclobutylamino	2-Cl-4-OMe-6-MePh	
	1496	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4-OMe-6-MePh	
10	1497	C-Me	N(Et)CH ₂ c-Pr	2-Cl-4-OMe-6-MePh	
	1498	C-Me	N(Pr)CH ₂ c-Pr	2-Cl-4-OMe-6-MePh	
	1499	C-Me	N(Me)Pr	2-Cl-4-OMe-6-MePh	
	1500	C-Me	N(Me)Et	2-Cl-4-OMe-6-MePh	
	1501	C-Me	N(Me)Bu	2-Cl-4-OMe-6-MePh	
15	1502	C-Me	N(Me)propargyl	2-Cl-4-OMe-6-MePh	
	1503	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4-OMe-6-MePh	
	1504	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4-OMe-6-MePh	
	1505	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4-OMe-6-MePh	
	1506	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4-OMe-6-MePh	
20	1507	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4-OMe-6-MePh	
	1508	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Cl-4-OMe-6-MePh	
	1509	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4-OMe-6-MePh	
	1510	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-6-MePh	
	1511	C-Me	NHCH(Et) ₂	2-Cl-4-OMe-6-MePh	
25	1512	C-Me	N(Et) ₂	2-Cl-4-OMe-6-MePh	
	1513	C-Me	NEt(Bu)	2-Cl-4-OMe-6-MePh	
	1514	C-Me	2-ethylpiperidyl	6-Me ₂ N-4-Me-	
				pyrid-3-yl	
	1515	C-Me	cyclobutylamino	6-Me ₂ N-4-Me-	
30				pyrid-3-yl	
	1516	C-Me	N(Me)CH ₂ CH=CH ₂	6-Me ₂ N-4-Me-	
				pyrid-3-yl	

	1517	C-Me	N(Et)CH ₂ C-Pr	6-Me ₂ N-4-Me-pyrid-3-yl
	1518	C-Me	N(Pr)CH ₂ C-Pr	6-Me ₂ N-4-Me-pyrid-3-yl
5	1519	C-Me	N(Me)Pr	6-Me ₂ N-4-Me-pyrid-3-yl
	1520	C-Me	N(Me)Et	6-Me ₂ N-4-Me-pyrid-3-yl
	1521	C-Me	N(Me)Bu	6-Me ₂ N-4-Me-pyrid-3-yl
10	1522	C-Me	N(Me)propargyl	6-Me ₂ N-4-Me-pyrid-3-yl
	1523	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	6-Me ₂ N-4-Me-pyrid-3-yl
15	1524	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	6-Me ₂ N-4-Me-pyrid-3-yl
	1525	C-Me	N(CH ₂ CH ₂ OMe)Me	6-Me ₂ N-4-Me-pyrid-3-yl
	1526 ^{at}	C-Me	N(CH ₂ CH ₂ OMe)Et	6-Me ₂ N-4-Me-pyrid-3-yl oil
20	1527	C-Me	N(CH ₂ CH ₂ OMe)Pr	6-Me ₂ N-4-Me-pyrid-3-yl
	1528	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	6-Me ₂ N-4-Me-pyrid-3-yl
25	1529	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	6-Me ₂ N-4-Me-pyrid-3-yl
	1530	C-Me	NHCH(c-Pr) ₂	6-Me ₂ N-4-Me-pyrid-3-yl
	1531 ^{au}	C-Me	N(CH ₂ CH ₂ OMe) ₂	6-Me ₂ N-4-Me-pyrid-3-yl
30				103-104
	1532 ^{av}	C-Me	NHCH(Et) ₂	6-Me ₂ N-4-Me-

			pyrid-3-yl	
			153 - 154	
1533 ^{aw}	C-Me	N(Et) ₂	6-Me ₂ N-4-Me- pyrid-3-yl	
5			117 - 118	
1534	C-Me	2-ethylpiperidyl	6-MeO-4-Me- pyrid-3-yl	
1535	C-Me	cyclobutylamino	6-MeO-4-Me- pyrid-3-yl	
10	1536	C-Me	N(Me)CH ₂ CH=CH ₂	6-MeO-4-Me- pyrid-3-yl
1537	C-Me	N(Et)CH ₂ c-Pr	6-MeO-4-Me- pyrid-3-yl	
1538	C-Me	N(Pr)CH ₂ c-Pr	6-MeO-4-Me- pyrid-3-yl	
15	1539	C-Me	N(Me)Pr	6-MeO-4-Me- pyrid-3-yl
1540	C-Me	N(Me)Et	6-MeO-4-Me- pyrid-3-yl	
20	1541	C-Me	N(Me)Bu	6-MeO-4-Me- pyrid-3-yl
1542	C-Me	N(Me)propargyl	6-MeO-4-Me- pyrid-3-yl	
1543	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	6-MeO-4-Me- pyrid-3-yl	
25	1544	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	6-MeO-4-Me- pyrid-3-yl
1545	C-Me	N(CH ₂ CH ₂ OMe)Me	6-MeO-4-Me- pyrid-3-yl	
30	1546	C-Me	N(CH ₂ CH ₂ OMe)Et	6-MeO-4-Me- pyrid-3-yl
1547	C-Me	N(CH ₂ CH ₂ OMe)Pr	6-MeO-4-Me- pyrid-3-yl	

	1548	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	6-MeO-4-Me-pyrid-3-yl
	1549	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	6-MeO-4-Me-pyrid-3-yl
5	1550	C-Me	NHCH(C-Pr) ₂	6-MeO-4-Me-pyrid-3-yl
	1551	C-Me	N(CH ₂ CH ₂ OMe) ₂	6-MeO-4-Me-pyrid-3-yl
	1552	C-Me	NHCH(Et) ₂	6-MeO-4-Me-pyrid-3-yl
10	1553	C-Me	N(Et) ₂	6-MeO-4-Me-pyrid-3-yl
	1554	C-Me	2-ethylpiperidyl	4,6-Me ₂ -pyrid-3-yl
15	1555	C-Me	cyclobutylamino	4,6-Me ₂ -pyrid-3-yl
	1556	C-Me	N(Me)CH ₂ CH=CH ₂	4,6-Me ₂ -pyrid-3-yl
	1557	C-Me	N(Et)CH ₂ C-Pr	4,6-Me ₂ -pyrid-3-yl
20	1558	C-Me	N(Pr)CH ₂ C-Pr	4,6-Me ₂ -pyrid-3-yl
	1559	C-Me	N(Me)Pr	4,6-Me ₂ -pyrid-3-yl
25	1560	C-Me	N(Me)Et	4,6-Me ₂ -pyrid-3-yl
	1561	C-Me	N(Me)Bu	4,6-Me ₂ -pyrid-3-yl
	1562	C-Me	N(Me)propargyl	4,6-Me ₂ -pyrid-3-yl
30	1563	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	4,6-Me ₂ -pyrid-3-yl

	1564	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	4,6-Me ₂ -pyrid-3-yl
	1565	C-Me	N(CH ₂ CH ₂ OMe)Me	4,6-Me ₂ -pyrid-3-yl
5	1566	C-Me	N(CH ₂ CH ₂ OMe)Et	4,6-Me ₂ -pyrid-3-yl
	1567	C-Me	N(CH ₂ CH ₂ OMe)Pr	4,6-Me ₂ -pyrid-3-yl
10	1568	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	4,6-Me ₂ -pyrid-3-yl
	1569	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	4,6-Me ₂ -pyrid-3-yl
	1570	C-Me	NHCH(c-Pr) ₂	4,6-Me ₂ -pyrid-3-yl
15	1571	C-Me	N(CH ₂ CH ₂ OMe) ₂	4,6-Me ₂ -pyrid-3-yl
	1572	C-Me	NHCH(Et) ₂	4,6-Me ₂ -pyrid-3-yl
	1573	C-Me	N(Et) ₂	4,6-Me ₂ -pyrid-3-yl
20	1574	C-Me	2-ethylpiperidyl	2,6-Me ₂ -pyrid-3-yl
	1575	C-Me	cyclobutylamino	2,6-Me ₂ -pyrid-3-yl
25	1576	C-Me	N(Me)CH ₂ CH=CH ₂	2,6-Me ₂ -pyrid-3-yl
	1577	C-Me	N(Et)CH ₂ C-Pr	2,6-Me ₂ -pyrid-3-yl
	1578	C-Me	N(Pr)CH ₂ C-Pr	2,6-Me ₂ -pyrid-3-yl
30	1579	C-Me	N(Me)Pr	2,6-Me ₂ -pyrid-3-yl

	1580	C-Me	N(Me)Et	2,6-Me ₂ - pyrid-3-yl
	1581	C-Me	N(Me)Bu	2,6-Me ₂ - pyrid-3-yl
5	1582	C-Me	N(Me)propargyl	2,6-Me ₂ - pyrid-3-yl
	1583	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2,6-Me ₂ - pyrid-3-yl
10	1584	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2,6-Me ₂ - pyrid-3-yl
	1585	C-Me	N(CH ₂ CH ₂ OMe)Me	2,6-Me ₂ - pyrid-3-yl
	1586	C-Me	N(CH ₂ CH ₂ OMe)Et	2,6-Me ₂ - pyrid-3-yl
15	1587	C-Me	N(CH ₂ CH ₂ OMe)Pr	2,6-Me ₂ - pyrid-3-yl
	1588	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2,6-Me ₂ - pyrid-3-yl
20	1589	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2,6-Me ₂ - pyrid-3-yl
	1590	C-Me	NHCH(c-Pr) ₂	2,6-Me ₂ - pyrid-3-yl
	1591	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,6-Me ₂ - pyrid-3-yl
25	1592	C-Me	NHCH(Et) ₂	2,6-Me ₂ - pyrid-3-yl
	1593	C-Me	N(Et) ₂	2,6-Me ₂ - pyrid-3-yl
	1594	C-Me	2-ethylpiperidyl	4-MeO-6-Me- pyrid-3-yl
30	1595	C-Me	cyclobutylamino	4-MeO-6-Me- pyrid-3-yl
	1596	C-Me	N(Me)CH ₂ CH=CH ₂	4-MeO-6-Me-

			pyrid-3-yl
1597	C-Me	N(Et)CH ₂ C-Pr	4-MeO-6-Me-
			pyrid-3-yl
1598	C-Me	N(Pr)CH ₂ C-Pr	4-MeO-6-Me-
5			pyrid-3-yl
1599	C-Me	N(Me)Pr	4-MeO-6-Me-
			pyrid-3-yl
1600	C-Me	N(Me)Et	4-MeO-6-Me-
10	1601	C-Me	pyrid-3-yl
		N(Me)Bu	4-MeO-6-Me-
	1602	C-Me	pyrid-3-yl
		N(Me)propargyl	4-MeO-6-Me-
15	1603	C-Me	pyrid-3-yl
		NH(CH(CH ₃)CH(CH ₃)CH ₃)	4-MeO-6-Me-
1604	C-Me		pyrid-3-yl
		N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	4-MeO-6-Me-
	1605	C-Me	pyrid-3-yl
20	1606	C-Me	4-MeO-6-Me-
		N(CH ₂ CH ₂ OMe)Et	pyrid-3-yl
	1607	C-Me	4-MeO-6-Me-
		N(CH ₂ CH ₂ OMe)Pr	pyrid-3-yl
25	1608	C-Me	4-MeO-6-Me-
		N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	pyrid-3-yl
1609	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	4-MeO-6-Me-
			pyrid-3-yl
1610	C-Me	NHCH(c-Pr) ₂	4-MeO-6-Me-
30	1611	C-Me	pyrid-3-yl
		N(CH ₂ CH ₂ OMe) ₂	4-MeO-6-Me-
	1612	C-Me	pyrid-3-yl
		NHCH(Et) ₂	4-MeO-6-Me-
			pyrid-3-yl

	1613	C-Me	N(Et) ₂	4-MeO-6-Me- pyrid-3-yl
	1614	C-Me	2-ethylpiperidyl	2-Br-4,5-(OMe) ₂ Ph
	1615	C-Me	cyclobutylamino	2-Br-4,5-(OMe) ₂ Ph
5	1616	C-Me	N(Me)CH ₂ CH=CH ₂	2-Br-4,5-(OMe) ₂ Ph
	1617	C-Me	N(Et)CH ₂ c-Pr	2-Br-4,5-(OMe) ₂ Ph
	1618	C-Me	N(Pr)CH ₂ c-Pr	2-Br-4,5-(OMe) ₂ Ph
	1619	C-Me	N(Me)Pr	2-Br-4,5-(OMe) ₂ Ph
	1620	C-Me	N(Me)Et	2-Br-4,5-(OMe) ₂ Ph
10	1621	C-Me	N(Me)Bu	2-Br-4,5-(OMe) ₂ Ph
	1622	C-Me	N(Me)propargyl	2-Br-4,5-(OMe) ₂ Ph
	1623	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Br-4,5-(OMe) ₂ Ph
	1624	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Br-4,5-(OMe) ₂ Ph
	1625	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Br-4,5-(OMe) ₂ Ph
15	1626	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Br-4,5-(OMe) ₂ Ph
	1627	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Br-4,5-(OMe) ₂ Ph
	1628	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Br-4,5-(OMe) ₂ Ph
	1629	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Br-4,5-(OMe) ₂ Ph
	1630	C-Me	NHCH(c-Pr) ₂	2-Br-4,5-(OMe) ₂ Ph
20	1631	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(OMe) ₂ Ph
	1632	C-Me	NHCH(Et) ₂	2-Br-4,5-(OMe) ₂ Ph
	1633	C-Me	N(Et) ₂	2-Br-4,5-(OMe) ₂ Ph
	1634	C-Me	NEt(Bu)	2-Br-4,5-(OMe) ₂ Ph

25 Notes for Table 7:

- a) CI-MS: 330 (M + H)⁺;
- b) CI-MS: 338 (M + H)⁺;
- c) CI-MS: 338 (M + H)⁺;
- d) CI-MS: 400 (M + H)⁺;
- 30 e) CI-MS: 326 (M + H)⁺;
- f) CI-MS: 354 (M + H)⁺;

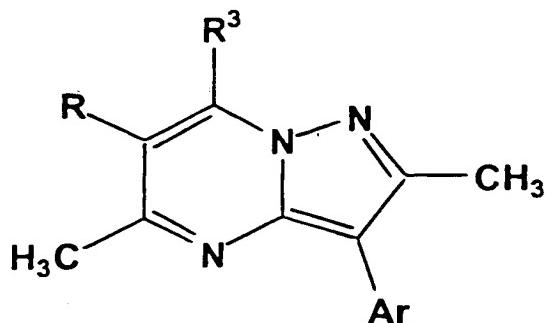
- h) CI-MS: 336 (M + H)⁺;
- i) CI-MS: 354 (M + H)⁺;
- j) CI-MS: 378 (M + H)⁺;
- k) CI-HRMS: Calcd 356.2087 (M + H)⁺, Found: 356.2071;
- 5 m) CI-MS: 340 (M + H)⁺;
- n) CI-MS: 368 (M + H)⁺;
- o) CI-MS: 326 (M + H)⁺;
- p) CI-MS: 368 (M + H)⁺;
- q) CI-MS: 394 (M + H)⁺;
- 10 r) CI-HRMS: Calcd 380.2087 (M + H)⁺, Found: 380.2078;
- s) CI-HRMS: Calcd 356.2008 (M + H)⁺, Found: 356.1997;
- t) CI-HRMS: Calcd 416.2220 (M + H)⁺, Found: 416.2005;
- u) CI-HRMS: Calcd 370.2243 (M + H)⁺, Found: 370.2246;
- v) CI-HRMS: Calcd 380.2400 (M + H)⁺, Found: 384.2382;
- 15 w) CI-HRMS: Calcd 429.2376 (M + H)⁺, Found: 429.2358;
- x) CI-HRMS: Calcd 397.2478 (M + H)⁺, Found: 397.2484;
- y) CI-HRMS: Calcd 410.5438 (M + H)⁺, Found: 410.2558;
- z) CI-HRMS: Calcd 368.4625 (M + H)⁺, Found: 368.2100;
- aa) CI-HRMS: Calcd 368.2090 (M + H)⁺, Found: 368.4625;
- 20 ab) CI-MS 410 (M + H)⁺;
- ac) CI-HRMS: Calcd 370.4785 (M + H)⁺, Found: 370.2246;
- ad) CI-HRMS: Calcd 356.4514 (M + H)⁺, Found: 356.2086;
- ae) CI-MS 384 (M + H)⁺;
- af) CI-MS 400 (M + H)⁺;
- 25 ag) CI-MS 426 (M + H)⁺;
- ah) CI-HRMS: Calcd 388.1553 (M + H)⁺, Found: 388.1554;
- ai) CI-HRMS: Calcd 388.1540 (M + H)⁺, Found: 358.1546;
- aj) CI-HRMS: Calcd 430.2005 (M + H)⁺, Found: 430.2006;
- ak) CI-HRMS: Calcd 390.1683 (M + H)⁺, Found: 390.1682;
- 30 al) CI-HRMS: Calcd 376.1554 (M + H)⁺, Found: 376.1548;
- am) CI-HRMS: Calcd 404.1853 (M + H)⁺, Found: 404.1850;
- an) CI-HRMS: Calcd 420.1810 (M + H)⁺, Found: 420.1809;

ao) CI-HRMS: Calcd 446.1946 (M + H)⁺, Found: 446.1949;
ap) CI-HRMS: Calcd 450.1917 (M + H)⁺, Found: 450.1913;
aq) CI-HRMS: Calcd 404.1839 (M + H)⁺, Found: 404.1846;
ar) CI-HRMS: Calcd 390.1678 (M + H)⁺, Found: 390.1680;
5 as) CI-HRMS: Calcd 418.2010 (M + H)⁺, Found: 418.2012;
at) CI-HRMS: Calcd 384.2512 (M + H)⁺, Found: 384.2506;
au) CI-HRMS: Calcd 414.2617 (M + H)⁺, Found: 414.2600;
av) CI-HRMS: Calcd 367.2484 (M + H)⁺, Found: 367.2477;
aw) CI-HRMS: Calcd 354.2406 (M + H)⁺, Found: 354.2388;
10 ax) CI-MS 370 (M + H)⁺;
ay) CI-MS 380 (M + H)⁺;
az) CI-MS 340 (M + H)⁺;
ba) CI-HRMS: Calcd 376.1340 (M + H)⁺, Found: 376.1347;
bb) CI-HRMS: Calcd 378.1497 (M + H)⁺, Found: 378.1495;
15 bc) CI-HRMS: Calcd 364.1340 (M + H)⁺, Found: 364.1333;
bd) CI-HRMS: Calcd 378.1593 (M + H)⁺, Found: 378.1498;
be) CI-HRMS: Calcd 392.1653 (M + H)⁺, Found: 392.1649;
bf) CI-HRMS: Calcd 378.1497 (M + H)⁺, Found: 378.1489;
bg) CI-HRMS: Calcd 406.1810 (M + H)⁺, Found: 406.1819;

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The examples delineated in TABLE 8 may be prepared by
the methods outlined in Examples 1A, 1B, 432, 433, 434.
Commonly used abbreviations are: Ph is phenyl, Pr is
25 propyl, Me is methyl, Et is ethyl, Bu is butyl, cPr is
cyclopropyl, Ex is Example, EtOAc is ethyl acetate.

TABLE 8



<u>Ex.</u>	<u>R</u>	<u>R³</u>	<u>Ar</u>	<u>mp (°C)</u>
5	2000	Me	$\text{N}(\text{CH}_2\text{CH}_2\text{OMe})_2$	2,4-Cl ₂ -Ph
	2001	Me	$\text{N}(\text{Bu})\text{Et}$	2,4-Cl ₂ -Ph
	2002	Me	$\text{NHCH}(\text{Et})\text{CH}_2\text{OMe}$	2,4-Cl ₂ -Ph
	2003	Me	$\text{N}(\text{Pr})\text{CH}_2\text{CH}_2\text{CN}$	2,4-Cl ₂ -Ph
	2004	Me	NH-3-pentyl	2,4-Cl ₂ -Ph
10	2005	Me	$\text{NHCH}(\text{CH}_2\text{OMe})_2$	2,4-Cl ₂ -Ph
	2006	Me	$\text{NHCH}(\text{Et})_2$	2,4-Me ₂ -Ph
	2007	Me	$\text{NHCH}(\text{CH}_2\text{OMe})_2$	2,4-Me ₂ -Ph
	2008	Me	$\text{N}(\text{CH}_2\text{CH}_2\text{OMe})_2$	2,4-Me ₂ -Ph
	2009	Me	$\text{N}(\text{c-Pr})\text{CH}_2\text{CH}_2\text{CN}$	2,4-Me ₂ -Ph
15	2010	Me	$\text{N}(\text{CH}_2\text{CH}_2\text{OMe})_2$	2-Cl,4-MePh
	2011	Me	$\text{NHCH}(\text{CH}_2\text{OMe})_2$	2-Cl,4-MePh
	2012	Me	$\text{NHCH}(\text{Et})_2$	2-Cl,4-MePh
	2013	Me	NEt ₂	2,4-Me ₂ -Ph
	2014	Me	$\text{N}(\text{Pr})\text{CH}_2\text{CH}_2\text{CN}$	2,4-Me ₂ -Ph
20	2015	Me	$\text{N}(\text{Bu})\text{CH}_2\text{CH}_2\text{CN}$	2,4-Me ₂ -Ph
	2016	Me	$\text{NHCH}(\text{Et})\text{CH}_2\text{OMe}$	2,4-Me ₂ -Ph
	2017	Me	$\text{NHCH}(\text{Et})_2$	2-Me,4-MeOPh
	2018	Me	$\text{NHCH}(\text{CH}_2\text{OMe})_2$	2-Me,4-MeOPh
	2019	Me	$\text{N}(\text{CH}_2\text{CH}_2\text{OMe})_2$	2-Me,4-MeOPh 115-
25	116 ^a			
	2020	Me	(S)-NHCH(CH ₂ CH ₂ OMe)-	2-Me,4-MeOPh

	2021		(CH ₂ OMe)	
	2022	Me	(S) -NHCH(CH ₂ CH ₂ OMe) -	2, 4-Me ₂ -Ph
	2023		(CH ₂ OMe)	
	2024	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me, 4-ClPh
5	2025	Me	NHET	2, 4-Me ₂ -Ph
	2026	Me	NHCH(Et) ₂	2-Me, 4-ClPh
	2027	Me	NHCH(CH ₂ OMe) ₂	2-Me, 4-ClPh
	2028	Me	N(Ac)Et	2, 4-Me ₂ -Ph
	2029	Me	(S) -NHCH(CH ₂ CH ₂ OMe) -	2-Me, 4-ClPh
	10	2030	(CH ₂ OMe)	
		2031	N(Pr)CH ₂ CH ₂ CN	2-Me, 4-MeOPh
		2032	NEt ₂	2-Me, 4-MeOPh
		2033	(S) -NHCH(CH ₂ CH ₂ OMe) -	2-Cl, 4-MePh
		2034	(CH ₂ OMe)	
15	2035	Me	NEt ₂	2-Cl, 4-MePh
	2036	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me, 4-MeOPh
	2037	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl, 4-MePh
	2038	Me	NHCH(Et)CH ₂ OMe	2-Me, 4-MeOPh
	2039	Me	NHCH(Et)CH ₂ OMe	2-Cl, 4-MePh
20	2040	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh
	2041	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh
	2042	Me	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh
	2043	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh
	2044	Me	NEt ₂	2-Cl-4-MeOPh
25	2045	Me	NH-3-pentyl	2-Cl-4-MeOPh
	2046	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	2047	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	2048	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	2049	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
30	2050	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2051	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2052	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4, 5-(MeO) ₂ Ph

	2053	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(MeO) ₂ Ph
	2054	Me	NHCH(Et)CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	2055	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,5-(MeO) ₂ Ph
	2056	Me	NET ₂	2-Cl-4,5-(MeO) ₂ Ph
5	2057	Me	NH-3-pentyl	2-Cl-4,5-(MeO) ₂ Ph
	2058	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	2059	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	2060	Me	NHCH(CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
	2061	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
10	2062	Me	NHCH(Et)CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
	2063	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,5-(MeO) ₂ Ph
	2064	Me	NET ₂	2-Br-4,5-(MeO) ₂ Ph
	2065	Me	NH-3-pentyl	2-Br-4,5-(MeO) ₂ Ph
	2066	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
15	2067	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
	2068	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
	2069	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
	2070	Me	NHCH(Et)CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
	2071	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,6-(MeO) ₂ Ph
20	2072	Me	NET ₂	2-Cl-4,6-(MeO) ₂ Ph
	2073	Me	NH-3-pentyl	2-Cl-4,6-(MeO) ₂ Ph
	2074	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
	2075	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
	2076	Me	NHCH(CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph
25	2077	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph
	2078	Me	NHCH(Et)CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2079	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4,6-(MeO) ₂ Ph
	2080	Me	NET ₂	2-Me-4,6-(MeO) ₂ Ph
	2081	Me	NH-3-pentyl	2-Me-4,6-(MeO) ₂ Ph
30	2082	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2083	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2084	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,6-(MeO) ₂ Ph

2085	Me	N <i>Et</i> ₂	2-Br-4,6-(MeO) ₂ Ph	
2086	Me	NH-3-pentyl	2-Br-4,6-(MeO) ₂ Ph	
2087	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph	
2088	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph	
5	2089	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
	2090	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
	2091	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh	
	2092	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh	
	2093	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh	
10	2094	N(<i>c</i> -Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh	
	2095	N <i>Et</i> ₂	2-MeO-4-MePh	
	2096	NH-3-pentyl	2-MeO-4-MePh	
	2097	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
	2098	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
15	2099	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh	
	2100	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh	
	2101	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh	
	2102	N(<i>c</i> -Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh	
	2103	N <i>Et</i> ₂	2-MeO-4-MePh	
20	2104	NH-3-pentyl	2-MeO-4-MePh	
	2105	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
	2106	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
	2107	NHCH(CH ₂ OMe) ₂	2-MeO-4-ClPh	
	2108	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-ClPh	
25	2109	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh	
	2110	N(<i>c</i> -Pr)CH ₂ CH ₂ CN	2-MeO-4-ClPh	
	2111	N <i>Et</i> ₂	2-MeO-4-ClPh	
	2112	NH-3-pentyl	2-MeO-4-ClPh	
	2113	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-ClPh	
30	2114	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-ClPh	
	2115	N(CH ₂ CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	
	2116	N(Bu)Et	2,4-Cl ₂ -Ph	

	2117	Cl	NHCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph
	2118	Cl	N(Pr)CH ₂ CH ₂ CN	2,4-Cl ₂ -Ph
	2119	Cl	NH-3-pentyl	2,4-Cl ₂ -Ph
	2120	Cl	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph
5	2121	Cl	NHCH(Et) ₂	2,4-Me ₂ -Ph
	2122	Cl	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	2123	Cl	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	2124	Cl	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	2125	Cl	N(CH ₂ CH ₂ OMe) ₂	2-Cl,4-MePh
	2126	Cl	NHCH(CH ₂ OMe) ₂	2-Cl,4-MePh
	2127	Cl	NHCH(Et) ₂	2-Cl,4-MePh
	2128	Cl	NEt ₂	2,4-Me ₂ -Ph
	2129	Cl	N(Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	2130	Cl	N(Bu)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
15	2131	Cl	NHCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph
	2132	Cl	NHCH(Et) ₂	2-Me,4-MeOPh
	2133	Cl	NHCH(CH ₂ OMe) ₂	2-Me,4-MeOPh
	2134	Cl	N(CH ₂ CH ₂ OMe) ₂	2-Me,4-MeOPh
20	2135	Cl	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me,4-MeOPh
	2136	Cl	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2,4-Me ₂ -Ph
	2137	Cl	N(CH ₂ CH ₂ OMe) ₂	2-Me,4-ClPh
	2138	Cl	NHET	2,4-Me ₂ -Ph
	2139	Cl	NHCH(Et) ₂	2-Me,4-ClPh
25	2140	Cl	NHCH(CH ₂ OMe) ₂	2-Me,4-ClPh
	2141	Cl	NHCH(CH ₂ OMe) ₂	2-Me,4-ClPh
	2142	Cl	NHCH(CH ₂ OMe) ₂	2-Me,4-ClPh
	2143	Cl	N(Ac)Et	2,4-Me ₂ -Ph
	2144	Cl	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me,4-ClPh
	2145	Cl	N(Pr)CH ₂ CH ₂ CN	2-Me,4-MeOPh
	2146	Cl	NEt ₂	2-Me,4-MeOPh
30	2147	Cl		

	2148	C1	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Cl, 4-MePh
	2149			
	2150	C1	NET ₂	2-Cl, 4-MePh
	2151	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Me, 4-MeOPh
5	2152	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Cl, 4-MePh
	2153	C1	NHCH(Et)CH ₂ OMe	2-Me, 4-MeOPh
	2154	C1	NHCH(Et)CH ₂ OMe	2-Cl, 4-MePh
	2155	C1	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh
	2156	C1	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh
10	2157	C1	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh
	2158	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh
	2159	C1	NET ₂	2-Cl-4-MeOPh
	2160	C1	NH-3-pentyl	2-Cl-4-MeOPh
	2161	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
15	2162	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	2163	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	2164	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh /
	2165	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2166	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
20	2167	C1	NHCH(CH ₂ OMe) ₂	2-Cl-4, 5-(MeO) ₂ Ph
	2168	C1	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4, 5-(MeO) ₂ Ph
	2169	C1	NHCH(Et)CH ₂ OMe	2-Cl-4, 5-(MeO) ₂ Ph
	2170	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4, 5-(MeO) ₂ Ph
	2171	C1	NET ₂	2-Cl-4, 5-(MeO) ₂ Ph
25	2172	C1	NH-3-pentyl	2-Cl-4, 5-(MeO) ₂ Ph
	2173	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO) ₂ Ph
	2174	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO) ₂ Ph
	2175	C1	NHCH(CH ₂ OMe) ₂	2-Br-4, 5-(MeO) ₂ Ph
	2176	C1	N(CH ₂ CH ₂ OMe) ₂	2-Br-4, 5-(MeO) ₂ Ph
30	2177	C1	NHCH(Et)CH ₂ OMe	2-Br-4, 5-(MeO) ₂ Ph
	2178	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4, 5-(MeO) ₂ Ph
	2179	C1	NET ₂	2-Br-4, 5-(MeO) ₂ Ph

	2180	C1	NH-3-pentyl	2-Br-4,5-(MeO) ₂ Ph
	2181	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
	2182	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
	2183	C1	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
5	2184	C1	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
	2185	C1	NHCH(Et)CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
	2186	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,6-(MeO) ₂ Ph
	2187	C1	NEt ₂	2-Cl-4,6-(MeO) ₂ Ph
	2188	C1	NH-3-pentyl	2-Cl-4,6-(MeO) ₂ Ph
	2189	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
10	2190	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
	2191	C1	NHCH(CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph
	2192	C1	N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph
	2193	C1	NHCH(Et)CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2194	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4,6-(MeO) ₂ Ph
	2195	C1	NEt ₂	2-Me-4,6-(MeO) ₂ Ph
15	2196	C1	NH-3-pentyl	2-Me-4,6-(MeO) ₂ Ph
	2197	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2198	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2199	C1	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,6-(MeO) ₂ Ph
	2200	C1	NEt ₂	2-Br-4,6-(MeO) ₂ Ph
	2201	C1	NH-3-pentyl	2-Br-4,6-(MeO) ₂ Ph
20	2202	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph
	2203	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph
	2204	C1	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2205	C1	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2206	C1	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh
	2207	C1	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh
25	2208	C1	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
	2209	C1	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	2210	C1	NEt ₂	2-MeO-4-MePh
	2211	C1	NH-3-pentyl	2-MeO-4-MePh

2212	Cl	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
2213	Cl	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh	
2214	Cl	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh	
2215	Cl	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh	
5	2216	Cl	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
	2217	Cl	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	2218	Cl	NEt ₂	2-MeO-4-MePh
	2219	Cl	NH-3-pentyl	2-MeO-4-MePh
	2220	Cl	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh
10	2221	Cl	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	2222	Cl	NHCH(CH ₂ OMe) ₂	2-MeO-4-ClPh
	2223	Cl	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-ClPh
	2224	Cl	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh
	2225	Cl	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-ClPh
15	2226	Cl	NEt ₂	2-MeO-4-ClPh
	2227	Cl	NH-3-pentyl	2-MeO-4-ClPh
	2228	Cl	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
	2229	Cl	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
	2230	F	N(CH ₂ CH ₂ OMe) ₂	2,4-Cl ₂ -Ph
20	2231	F	N(Bu)Et	2,4-Cl ₂ -Ph
	2232	F	NHCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph
	2233	F	N(Pr)CH ₂ CH ₂ CN	2,4-Cl ₂ -Ph
	2234	F	NH-3-pentyl	2,4-Cl ₂ -Ph
	2235	F	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph
25	2236	F	NHCH(Et) ₂	2,4-Me ₂ -Ph
	2237	F	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	2238	F	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	2239	F	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	2240	F	N(CH ₂ CH ₂ OMe) ₂	2-Cl,4-MePh
30	2241	F	NHCH(CH ₂ OMe) ₂	2-Cl,4-MePh
	2242	F	NHCH(Et) ₂	2-Cl,4-MePh
	2243	F	NEt ₂	2,4-Me ₂ -Ph

		N(Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
		N(Bu)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
		NHCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph
		NHCH(Et) ₂	2-Me-4-MeOph
5	2248	NHCH(CH ₂ OMe) ₂	2-Me-4-MeOph
	2249	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-MeOph
	2250	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me-4-MeOph
	2252	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2,4-Me ₂ -Ph
10	2253	N(CH ₂ CH ₂ OMe) ₂	2-Me,4-ClPh
	2255	NHET	2,4-Me ₂ -Ph
	2256	NHCH(Et) ₂	2-Me,4-ClPh
	2257	NHCH(CH ₂ OMe) ₂	2-Me,4-ClPh
15	2258	N(Ac)Et	2,4-Me ₂ -Ph
	2259	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me,4-ClPh
	2261	N(Pr)CH ₂ CH ₂ CN	2-Me,4-MeOph
	2262	NET ₂	2-Me,4-MeOph
20	2263	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Cl,4-MePh
	2265	NET ₂	2-Cl,4-MePh
	2266	N(c-Pr)CH ₂ CH ₂ CN	2-Me,4-MeOph
	2267	N(c-Pr)CH ₂ CH ₂ CN	2-Cl,4-MePh
25	2268	NHCH(Et)CH ₂ OMe	2-Me,4-MeOph
	2269	NHCH(Et)CH ₂ OMe	2-Cl,4-MePh
	2270	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOph
	2271	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOph
	2272	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOph
30	2273	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOph
	2274	NET ₂	2-Cl-4-MeOph
	2275	NH-3-pentyi	2-Cl-4-MeOph

			NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
2276	F		NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
2277	F		NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
2278	F		NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
2279	F		NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
5	2280	F	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
2281	F		NHCH(CH ₂ OMe) ₂	2-Cl-4,5-(MeO) ₂ Ph
2282	F		N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(MeO) ₂ Ph
2283	F		NHCH(Et)CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
2284	F		N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,5-(MeO) ₂ Ph
10	2285	F	NEt ₂	2-Cl-4,5-(MeO) ₂ Ph
2286	F		NH-3-pentyl	2-Cl-4,5-(MeO) ₂ Ph
2287	F		NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
2288	F		NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
2289	F		NHCH(CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
15	2290	F	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
2291	F		NHCH(Et)CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
2292	F		N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,5-(MeO) ₂ Ph
2293	F		NEt ₂	2-Br-4,5-(MeO) ₂ Ph
20	2294	F	NH-3-pentyl	2-Br-4,5-(MeO) ₂ Ph
2295	F		NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
2296	F		NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
2297	F		NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
2298	F		N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
2299	F		NHCH(Et)CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
25	2300	F	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,6-(MeO) ₂ Ph
2301	F		NEt ₂	2-Cl-4,6-(MeO) ₂ Ph
2302	F		NH-3-pentyl	2-Cl-4,6-(MeO) ₂ Ph
2303	F		NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
2304	F		NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO) ₂ Ph
30	2305	F	NEt ₂	2-Cl-4,6-(MeO) ₂ Ph
2306	F		NHCH(CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph
2307	F		N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO) ₂ Ph

	2308	F	NHCH(Et)CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2309	F	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4,6-(MeO) ₂ Ph
	2310	F	NEt ₂	2-Me-4,6-(MeO) ₂ Ph
	2311	F	NH-3-pentyl	2-Me-4,6-(MeO) ₂ Ph
5	2312	F	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2313	F	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO) ₂ Ph
	2314	F	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,6-(MeO) ₂ Ph
	2315	F	NEt ₂	2-Br-4,6-(MeO) ₂ Ph
	2316	F	NH-3-pentyl	2-Br-4,6-(MeO) ₂ Ph
10	2317	F	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph
	2318	F	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO) ₂ Ph
	2319	F	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2320	F	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	2321	F	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh
15	2322	F	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh
	2323	F	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
	2324	F	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	2325	F	NEt ₂	2-MeO-4-MePh
	2326	F	NH-3-pentyl	2-MeO-4-MePh
20	2327	F	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	2328	F	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	2329	F	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh
	2330	F	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh
	2331	F	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
25	2332	F	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	2333	F	NEt ₂	2-MeO-4-MePh
	2334	F	NH-3-pentyl	2-MeO-4-MePh
	2335	F	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	2336	F	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh
30	2337	F	NHCH(CH ₂ OMe) ₂	2-MeO-4-ClPh
	2338	F	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-ClPh
	2339	F	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh

	2340	F	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-ClPh
	2341	F	NEt ₂	2-MeO-4-ClPh
	2342	F	NH-3-pentyl	2-MeO-4-ClPh
	2343	F	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
5	2344	F	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
	2345	Me	NMe(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2346	Me	NEt(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2347	Me	NPr(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2348	Me	NH-2-butyl	2,4-Cl ₂ -Ph
	10 2349	Me	cyclobutylamino	2,4-Cl ₂ -Ph
	2350	Me	2-ethylpiperidinyl	2,4-Cl ₂ -Ph
	2351	Me	NMe(propargyl)	2,4-Cl ₂ -Ph
	2352	Me	NEt(propargyl)	2,4-Cl ₂ -Ph
	2353	Me	NEtMe	2,4-Cl ₂ -Ph
15	2354	Me	NEtPr	2,4-Cl ₂ -Ph
	2355	Me	NMeBu	2,4-Cl ₂ -Ph
	2356	Me	NMe(CH ₂ cPr)	2,4-Cl ₂ -Ph
	2357	Me	NEt(CH ₂ cPr)	2,4-Cl ₂ -Ph
	2358	Me	NPr(CH ₂ cPr)	2,4-Cl ₂ -Ph
20	2359	Me	NMe(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2360	Me	NEt(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2361	Me	NPr(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2362	Me	NH-2-butyl	2-Me-4-MeOPh
	2363	Me	cyclobutylamino	2-Me-4-MeOPh
	25 2364	Me	2-ethylpiperidinyl	2-Me-4-MeOPh
	2365	Me	NMe(propargyl)	2-Me-4-MeOPh
	2366	Me	NEt(propargyl)	2-Me-4-MeOPh
	2367	Me	NEtMe	2-Me-4-MeOPh
	2368	Me	NEtPr	2-Me-4-MeOPh
30	2369	Me	NMeBu	2-Me-4-MeOPh
	2370	Me	NMe(CH ₂ cPr)	2-Me-4-MeOPh
	2371	Me	NEt(CH ₂ cPr)	2-Me-4-MeOPh
	2372	Me	NPr(CH ₂ cPr)	2-Me-4-MeOPh

	2373	Me	NMe(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2374	Me	NEt(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2375	Me	NPr(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2376	Me	NH-2-butyl	2,4-Me ₂ -Ph
5	2377	Me	cyclobutylamino	2,4-Me ₂ -Ph
	2378	Me	2-ethylpiperidinyl	2,4-Me ₂ -Ph
	2379	Me	NMe(propargyl)	2,4-Me ₂ -Ph
	2380	Me	NEt(propargyl)	2,4-Me ₂ -Ph
	2381	Me	NETMe	2,4-Me ₂ -Ph
	2382	Me	NETPr	2,4-Me ₂ -Ph
10	2383	Me	NMeBu	2,4-Me ₂ -Ph
	2384	Me	NMe(CH ₂ cPr)	2,4-Me ₂ -Ph
	2385	Me	NEt(CH ₂ cPr)	2,4-Me ₂ -Ph
	2386	Me	NPr(CH ₂ cPr)	2,4-Me ₂ -Ph
	2387	Me	NMe(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2388	Me	NEt(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
15	2389	Me	NPr(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2390	Me	NH-2-butyl	2-Cl-4-MeOPh
	2391	Me	cyclobutylamino	2-Cl-4-MeOPh
	2392	Me	2-ethylpiperidinyl	2-Cl-4-MeOPh
	2393	Me	NMe(propargyl)	2-Cl-4-MeOPh
	2394	Me	NEt(propargyl)	2-Cl-4-MeOPh
20	2395	Me	NETMe	2-Cl-4-MeOPh
	2396	Me	NETPr	2-Cl-4-MeOPh
	2397	Me	NMeBu	2-Cl-4-MeOPh
	2398	Me	NMe(CH ₂ cPr)	2-Cl-4-MeOPh
	2399	Me	NEt(CH ₂ cPr)	2-Cl-4-MeOPh
	2400	Me	NPr(CH ₂ cPr)	2-Cl-4-MeOPh
25	2401	Me	NMe(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
	2402	Me	NEt(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
	2403	Me	NPr(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
	2404	Me	NH-2-butyl	2,5-Me ₂ -4-MeOPh

	2405	Me	cyclobutylamino	2,5-Me ₂ -4-MeOPh
	2406	Me	2-ethylpiperidinyl	2,5-Me ₂ -4-MeOPh
	2407	Me	NMe (propargyl)	2,5-Me ₂ -4-MeOPh
	2408	Me	NET (propargyl)	2,5-Me ₂ -4-MeOPh
5	2409	Me	NEtMe	2,5-Me ₂ -4-MeOPh
	2410	Me	NEtPr	2,5-Me ₂ -4-MeOPh
	2411	Me	NMeBu	2,5-Me ₂ -4-MeOPh
	2412	Me	NMe (CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	2413	Me	NET (CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	10	2414	NPr (CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	2415	Cl	NMe (CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2416	Cl	NET (CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2417	Cl	NPr (CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2418	Cl	NH-2-butyl	2,4-Cl ₂ -Ph
15	2419	Cl	cyclobutylamino	2,4-Cl ₂ -Ph
	2420	Cl	2-ethylpiperidinyl	2,4-Cl ₂ -Ph
	2421	Cl	NMe (propargyl)	2,4-Cl ₂ -Ph
	2422	Cl	NET (propargyl)	2,4-Cl ₂ -Ph
	2423	Cl	NEtMe	2,4-Cl ₂ -Ph
	20	2424	NEtPr	2,4-Cl ₂ -Ph
	2425	Cl	NMeBu	2,4-Cl ₂ -Ph
	2426	Cl	NMe (CH ₂ cPr)	2,4-Cl ₂ -Ph
	2427	Cl	NET (CH ₂ cPr)	2,4-Cl ₂ -Ph
	2428	Cl	NPr (CH ₂ cPr)	2,4-Cl ₂ -Ph
25	2429	Cl	NMe (CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2430	Cl	NET (CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2431	Cl	NPr (CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2432	Cl	NH-2-butyl	2-Me-4-MeOPh
	2433	Cl	cyclobutylamino	2-Me-4-MeOPh
	30	2434	2-ethylpiperidinyl	2-Me-4-MeOPh
	2435	Cl	NMe (propargyl)	2-Me-4-MeOPh
	2436	Cl	NET (propargyl)	2-Me-4-MeOPh

	2437	C1	NEtMe	2-Me-4-MeOPh
	2438	C1	NEtPr	2-Me-4-MeOPh
	2439	C1	NMeBu	2-Me-4-MeOPh
	2440	C1	NMe(CH ₂ cPr)	2-Me-4-MeOPh
5	2441	C1	NEt(CH ₂ cPr)	2-Me-4-MeOPh
	2442	C1	NPr(CH ₂ cPr)	2-Me-4-MeOPh
	2443	C1	NMe(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2444	C1	NEt(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2445	C1	NPr(CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
10	2446	C1	NH-2-buty1	2,4-Me ₂ -Ph
	2447	C1	cyclobutylamino	2,4-Me ₂ -Ph
	2448	C1	2-ethylpiperidinyl	2,4-Me ₂ -Ph
	2449	C1	NMe(propargyl)	2,4-Me ₂ -Ph
	2450	C1	NEt(propargyl)	2,4-Me ₂ -Ph
15	2451	C1	NEtMe	2,4-Me ₂ -Ph
	2452	C1	NEtPr	2,4-Me ₂ -Ph
	2453	C1	NMeBu	2,4-Me ₂ -Ph
	2454	C1	NMe(CH ₂ cPr)	2,4-Me ₂ -Ph
	2455	C1	NEt(CH ₂ cPr)	2,4-Me ₂ -Ph
20	2456	C1	NPr(CH ₂ cPr)	2,4-Me ₂ -Ph
	2457	C1	NMe(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2458	C1	NEt(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2459	C1	NPr(CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2460	C1	NH-2-buty1	2-Cl-4-MeOPh
25	2461	C1	cyclobutylamino	2-Cl-4-MeOPh
	2462	C1	2-ethylpiperidinyl	2-Cl-4-MeOPh
	2463	C1	NMe(propargyl)	2-Cl-4-MeOPh
	2464	C1	NEt(propargyl)	2-Cl-4-MeOPh
	2465	C1	NEtMe	2-Cl-4-MeOPh
30	2466	C1	NEtPr	2-Cl-4-MeOPh
	2467	C1	NMeBu	2-Cl-4-MeOPh
	2468	C1	NMe(CH ₂ cPr)	2-Cl-4-MeOPh
	2469	C1	NEt(CH ₂ cPr)	2-Cl-4-MeOPh

2470	Cl	NPr(CH ₂ cPr)	2-Cl-4-MeOPh
2471	Cl	NMe(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
2472	Cl	NEt(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
2473	Cl	NPr(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
5	2474	NH-2-butyl	2,5-Me ₂ -4-MeOPh
	2475	cyclobutylamino	2,5-Me ₂ -4-MeOPh
	2476	2-ethylpiperidinyl	2,5-Me ₂ -4-MeOPh
	2477	NMe(propargyl)	2,5-Me ₂ -4-MeOPh
	2478	NEt(propargyl)	2,5-Me ₂ -4-MeOPh
10	2479	NEtMe	2,5-Me ₂ -4-MeOPh
	2480	NEtPr	2,5-Me ₂ -4-MeOPh
	2481	NMeBu	2,5-Me ₂ -4-MeOPh
	2482	NMe(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	2483	NEt(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
15	2484	NPr(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	2485	NMe(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2486	NEt(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2487	NPr(CH ₂ CH ₂ OMe)	2,4-Cl ₂ -Ph
	2488	NH-2-butyl	2,4-Cl ₂ -Ph
20	2489	cyclobutylamino	2,4-Cl ₂ -Ph
	2490	2-ethylpiperidinyl	2,4-Cl ₂ -Ph
	2491	NMe(propargyl)	2,4-Cl ₂ -Ph
	2492	NEt(propargyl)	2,4-Cl ₂ -Ph
	2493	NEtMe	2,4-Cl ₂ -Ph
25	2494	NEtPr	2,4-Cl ₂ -Ph
	2495	NMeBu	2,4-Cl ₂ -Ph
	2496	NMe(CH ₂ cPr)	2,4-Cl ₂ -Ph
	2497	NEt(CH ₂ cPr)	2,4-Cl ₂ -Ph
	2498	NPr(CH ₂ cPr)	2,4-Cl ₂ -Ph
30	2499	NMe(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2500	NEt(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh
	2501	NPr(CH ₂ CH ₂ OMe)	2-Me-4-MeOPh

	2502	F	NH-2-butyl	2-Me-4-MeOPh
	2503	F	cyclobutylamino	2-Me-4-MeOPh
	2504	F	2-ethylpiperidinyl	2-Me-4-MeOPh
	2505	F	NMe (propargyl)	2-Me-4-MeOPh
5	2506	F	NEt (propargyl)	2-Me-4-MeOPh
	2507	F	NEtMe	2-Me-4-MeOPh
	2508	F	NEtPr	2-Me-4-MeOPh
	2509	F	NMeBu	2-Me-4-MeOPh
	2510	F	NMe (CH ₂ cPr)	2-Me-4-MeOPh
10	2511	F	NEt (CH ₂ cPr)	2-Me-4-MeOPh
	2512	F	NPr (CH ₂ cPr)	2-Me-4-MeOPh
	2513	F	NMe (CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2514	F	NEt (CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
	2515	F	NPr (CH ₂ CH ₂ OMe)	2,4-Me ₂ -Ph
15	2516	F	NH-2-butyl	2,4-Me ₂ -Ph
	2517	F	cyclobutylamino	2,4-Me ₂ -Ph
	2518	F	2-ethylpiperidinyl	2,4-Me ₂ -Ph
	2519	F	NMe (propargyl)	2,4-Me ₂ -Ph
	2520	F	NEt (propargyl)	2,4-Me ₂ -Ph
20	2521	F	NEtMe	2,4-Me ₂ -Ph
	2522	F	NEtPr	2,4-Me ₂ -Ph
	2523	F	NMeBu	2,4-Me ₂ -Ph
	2524	F	NMe (CH ₂ cPr)	2,4-Me ₂ -Ph
	2525	F	NEt (CH ₂ cPr)	2,4-Me ₂ -Ph
25	2526	F	NPr (CH ₂ cPr)	2,4-Me ₂ -Ph
	2527	F	NMe (CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2528	F	NEt (CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2529	F	NPr (CH ₂ CH ₂ OMe)	2-Cl-4-MeOPh
	2530	F	NH-2-butyl	2-Cl-4-MeOPh
30	2531	F	cyclobutylamino	2-Cl-4-MeOPh
	2532	F	2-ethylpiperidinyl	2-Cl-4-MeOPh
	2533	F	NMe (propargyl)	2-Cl-4-MeOPh
	2534	F	NEt (propargyl)	2-Cl-4-MeOPh

			NEtMe	2-Cl-4-MeOPh
			NEtPr	2-Cl-4-MeOPh
			NMeBu	2-Cl-4-MeOPh
			NMe(CH ₂ cPr)	2-Cl-4-MeOPh
5	2539	F	NEt(CH ₂ cPr)	2-Cl-4-MeOPh
	2540	F	NPr(CH ₂ cPr)	2-Cl-4-MeOPh
	2541	F	NMe(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
	2542	F	NEt(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
	2543	F	NPr(CH ₂ CH ₂ OMe)	2,5-Me ₂ -4-MeOPh
10	2544	F	NH-2-butyl	2,5-Me ₂ -4-MeOPh
	2545	F	cyclobutylamino	2,5-Me ₂ -4-MeOPh
	2546	F	2-ethylpiperidinyl	2,5-Me ₂ -4-MeOPh
	2547	F	NMe(propargyl)	2,5-Me ₂ -4-MeOPh
	2548	F	NEt(propargyl)	2,5-Me ₂ -4-MeOPh
15	2549	F	NEtMe	2,5-Me ₂ -4-MeOPh
	2550	F	NEtPr	2,5-Me ₂ -4-MeOPh
	2551	F	NMeBu	2,5-Me ₂ -4-MeOPh
	2552	F	NMe(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
	2553	F	NEt(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh
20	2554	F	NPr(CH ₂ cPr)	2,5-Me ₂ -4-MeOPh

a)CI-HRMS: Calcd: 367.2498; Found: 367.2468 (M + H)⁺

b)CI-HRMS: Calcd: 387.1952; Found: 387.1939 (M + H)⁺

25

Utility

CRF-R1 Receptor Binding Assay for the Evaluation of Biological Activity

30

The following is a description of the isolation of cell membranes containing cloned human CRF-R1 receptors for use in the standard binding assay

as well as a description of the assay itself.

Messenger RNA was isolated from human hippocampus. The mRNA was reverse transcribed using oligo (dt) 12-18 and the coding region was amplified by PCR from start to stop codons. The resulting PCR fragment was cloned into the EcoRV site of pGEMV, from whence the insert was reclaimed using XhoI + XbaI and cloned into the XhoI + XbaI sites of vector pm3ar (which contains a CMV promoter, the SV40 't' splice and early poly A signals, an Epstein-Barr viral origin of replication, and a hygromycin selectable marker). The resulting expression vector, called phchCRFR was transfected in 293EBNA cells and cells retaining the episome were selected in the presence of 400 µM hygromycin. Cells surviving 4 weeks of selection in hygromycin were pooled, adapted to growth in suspension and used to generate membranes for the binding assay described below. Individual aliquots containing approximately 1 x 10⁸ of the suspended cells were then centrifuged to form a pellet and frozen.

For the binding assay a frozen pellet described above containing 293EBNA cells transfected with hCRFR1 receptors is homogenized in 10 ml of ice cold tissue buffer (50 mM HEPES buffer pH 7.0, containing 10 mM MgCl₂, 2 mM EGTA, 1 µg/ml aprotinin, 1 µg/ml leupeptin and 1 µg/ml pepstatin). The homogenate is centrifuged at 40,000 x g for 12 min and the resulting pellet rehomogenized in 10 ml of tissue buffer. After another centrifugation at 40,000 x g for 12 min, the pellet is resuspended to a protein concentration of 360 µg/ml to be used in the assay.

Binding assays are performed in 96 well plates; each well having a 300 µl capacity. To each well is added 50 µl of test drug dilutions (final concentration

of drugs range from 10^{-10} - 10^{-5} M), 100 μ l of ^{125}I -ovine-CRF (^{125}I -o-CRF) (final concentration 150 pM) and 150 μ l of the cell homogenate described above. Plates are then allowed to incubate at room temperature for 2 hours before filtering the incubate over GF/F filters (presoaked with 0.3% polyethyleneimine) using an appropriate cell harvester. Filters are rinsed 2 times with ice cold assay buffer before removing individual filters and assessing them for radioactivity on a gamma counter.

Curves of the inhibition of ^{125}I -o-CRF binding to cell membranes at various dilutions of test drug are analyzed by the iterative curve fitting program LIGAND [P.J. Munson and D. Rodbard, *Anal. Biochem.* 107:220 (1980)], which provides K_i values for inhibition which are then used to assess biological activity.

A compound is considered to be active if it has a K_i value of less than about 10000 nM for the inhibition of CRF.

Inhibition of CRF-Stimulated Adenylate Cyclase Activity

Inhibition of CRF-stimulated adenylate cyclase activity can be performed as described by G. Battaglia et al. *Synapse* 1:572 (1987). Briefly, assays are carried out at 37° C for 10 min in 200 ml of buffer containing 100 mM Tris-HCl (pH 7.4 at 37° C), 10 mM MgCl₂, 0.4 mM EGTA, 0.1% BSA, 1 mM isobutylmethylxanthine (IBMX), 250 units/ml phosphocreatine kinase, 5 mM creatine phosphate, 100 mM guanosine 5'-triphosphate, 100 nM oCRF, antagonist peptides (concentration range 10^{-9} to 10^{-6} M) and 0.8 mg original wet weight tissue

(approximately 40-60 mg protein). Reactions are initiated by the addition of 1 mM ATP/[³²P]ATP (approximately 2-4 mCi/tube) and terminated by the addition of 100 ml of 50 mM Tris-HCL, 45 mM ATP and 5% sodium dodecyl sulfate. In order to monitor the recovery of cAMP, 1 μ l of [³H]cAMP (approximately 40,000 dpm) is added to each tube prior to separation. The separation of [³²P]cAMP from [³²P]ATP is performed by sequential elution over 10 Dowex and alumina columns.

In vivo Biological Assay

The *in vivo* activity of the compounds of the present invention can be assessed using any one of 15 the biological assays available and accepted within the art. Illustrative of these tests include the Acoustic Startle Assay, the Stair Climbing Test, and the Chronic Administration Assay. These and other models useful for the testing of compounds of the 20 present invention have been outlined in C.W. Berridge and A.J. Dunn *Brain Research Reviews* 15:71 (1990).

Compounds may be tested in any species of rodent or small mammal.

25 Compounds of this invention have utility in the treatment of imbalances associated with abnormal levels of corticotropin releasing factor in patients suffering from depression, affective disorders, 30 and/or anxiety.

Compounds of this invention can be administered to treat these abnormalities by means that produce contact of the active agent with the agent's site of action in the body of a mammal. The compounds can be

administered by any conventional means available for use in conjunction with pharmaceuticals either as individual therapeutic agent or in combination of therapeutic agents. They can be administered alone, 5 but will generally be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage administered will vary depending on 10 the use and known factors such as pharmacodynamic character of the particular agent, and its mode and route of administration; the recipient's age, weight, and health; nature and extent of symptoms; kind of concurrent treatment; frequency of 15 treatment; and desired effect. For use in the treatment of said diseases or conditions, the compounds of this invention can be orally administered daily at a dosage of the active ingredient of 0.002 to 200 mg/kg of body weight. 20 Ordinarily, a dose of 0.01 to 10 mg/kg in divided doses one to four times a day, or in sustained release formulation will be effective in obtaining the desired pharmacological effect.

Dosage forms (compositions) suitable for 25 administration contain from about 1 mg to about 100 mg of active ingredient per unit. In these pharmaceutical compositions, the active ingredient will ordinarily be present in an amount of about 0.5 to 95% by weight based on the total weight of the 30 composition.

The active ingredient can be administered orally in solid dosage forms, such as capsules, tablets and powders; or in liquid forms such as elixirs, syrups, 35 and/or suspensions. The compounds of this invention

can also be administered parenterally in sterile liquid dose formulations.

Gelatin capsules can be used to contain the active ingredient and a suitable carrier such as but not limited to lactose, starch, magnesium stearate, steric acid, or cellulose derivatives. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of time. Compressed tablets can be sugar-coated or film-coated to mask any unpleasant taste, or used to protect the active ingredients from the atmosphere, or to allow selective disintegration of the tablet in the gastrointestinal tract.

Liquid dose forms for oral administration can contain coloring or flavoring agents to increase patient acceptance.

In general, water, pharmaceutically acceptable oils, saline, aqueous dextrose (glucose), and related sugar solutions and glycols, such as propylene glycol or polyethylene glycol, are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents, such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or in combination, are suitable stabilizing agents. Also used are citric acid and its salts, and EDTA. In addition, parenteral solutions can contain preservatives such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described

in "Remington's Pharmaceutical Sciences", A. Osol, a standard reference in the field.

Useful pharmaceutical dosage-forms for administration of the compounds of this invention 5 can be illustrated as follows:

Capsules

A large number of units capsules are prepared by filling standard two-piece hard gelatin capsules 10 each with 100 mg of powdered active ingredient, 150 mg lactose, 50 mg cellulose, and 6 mg magnesium stearate.

Soft Gelatin Capsules

15 A mixture of active ingredient in a digestible oil such as soybean, cottonseed oil, or olive oil is prepared and injected by means of a positive displacement was pumped into gelatin to form soft gelatin capsules containing 100 mg of the active 20 ingredient. The capsules were washed and dried.

Tablets

A large number of tablets are prepared by conventional procedures so that the dosage unit was 25 100 mg active ingredient, 0.2 mg of colloidal silicon dioxide, 5 mg of magnesium stearate, 275 mg of microcrystalline cellulose, 11 mg of starch, and 98.8 mg lactose. Appropriate coatings may be applied to increase palatability or delayed 30 adsorption.

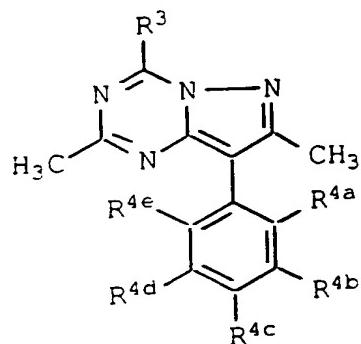
The compounds of this invention may also be used as reagents or standards in the biochemical study of neurological function, dysfunction, and 35 disease.

Although the present invention has been described and exemplified in terms of certain preferred embodiments, other embodiments will be apparent to those skilled in the art. The invention is, therefore, not limited to the particular embodiments described and exemplified, but is capable of modification or variation without departing from the spirit of the invention, the full scope of which is delineated by the appended claims.

CLAIMS

WHAT IS CLAIMED IS:

- 5 1. A compound of Formula (50)



FORMULA (50)

10

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof,

15 selected from the group:

a compound of Formula (50) wherein R³ is -NHCH(CH₂CH₂OMe)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

20 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is cyclobutyl-aminoc, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
 N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
 N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is N(Me)cEt, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;
- 35 a compound of Formula (50) wherein R³ is
 N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
 N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is

- OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)-CH_2CH=CH_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)Me$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)Et$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)Pr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R^3 is $NHCH(CH_3)CH_2CH_3$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R^3 is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
 N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 15 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is
 N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
 N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is

- Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 20 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(cPr)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 40 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 35 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is cyclobutyl-
amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
 N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
 N(Et)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;
- 35 a compound of Formula (50) wherein R³ is
 N(Me)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
 N(Et)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is

- OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is $N(Me)CH_2CH=CH_2$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is $N(Et)CH_2CH=CH_2$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R^3 is $N(Me)Pr$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R^3 is $N(Me)Et$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is $N(Me)propargyl$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
N(Et)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d}
is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is
Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and
R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and
R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}

- is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is $N(Et)_2$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R^3 is $N(Me)CH_2CH=CH_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R^3 is $N(Et)CH_2CH=CH_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R^3 is $N(Me)Pr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R^3 is $N(Me)Et$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

5 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

10 a compound of Formula (50) wherein R³ is
N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

15 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is Me;

20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is Me;

25 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

30 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

35 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
35 and R^{4e} is Me;

40 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}

- is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 5 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,

- R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2$,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)_2$,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R^3 is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R^3 is $N(Me)CH_2CH=CH_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$,

- R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is
 $N(CH_2CH_2OMe)Pr$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is $N(CH_2CH_2OMe)-$
 CH_2cPr , R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is
 $NHCH(CH_3)CH_2CH_3$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is $NHCH(cPr)_2$,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 20 a compound of Formula (50) wherein R³ is $N(CH_2CH_2OMe)_2$,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 25 a compound of Formula (50) wherein R³ is $NHCH(Et)_2$, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
OMe;
- 30 a compound of Formula (50) wherein R³ is $NHCH(Et)_2$, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 35 a compound of Formula (50) wherein R³ is 2-
ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
 $N(Me)CH_2CH=CH_2$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 15 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 30 a compound of Formula (50) wherein R³ is
N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
N(Et)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is

- H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 20 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 30 25 a compound of Formula (50) wherein R³ is NHCH(cPr)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 35 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;
- 40 35 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

- 5
- a compound of Formula (50) wherein R³ is
 $\text{NH}(\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}_3$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is
 $\text{N}(\text{CH}_2\text{CH}_2\text{OMe})\text{Me}$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
 $\text{N}(\text{CH}_2\text{CH}_2\text{OMe})\text{Et}$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is
 $\text{N}(\text{CH}_2\text{CH}_2\text{OMe})\text{Pr}$, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 $\text{NH}(\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$, R^{4a} is Cl, R^{4b} is F, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}

- is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 45 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

H;

- 5 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

5 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

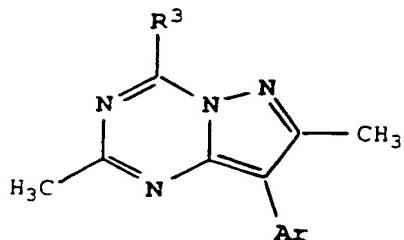
- a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a}
 is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
 H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a}
 is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
 H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a}
 is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
 H;
- 20 a compound of Formula (50) wherein R³ is
 N(Me)propargyl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 NH(CH(CH₃)CH(CH₃)CH₃, R^{4a} is Br, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 F and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is
 N(CH₂CH₂OMe)Me, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
 N(CH₂CH₂OMe)Et, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is
 N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R³ is
 N(CH₂CH₂OMe)cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is

- OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is
 $NH(CH(CH_3)CH_2CH_3, R^{4a}$ is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2,$
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is $N(CH_2CH_2OMe)_2,$
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2, R^{4a}$
is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 20 a compound of Formula (50) wherein R^3 is $N(Et)_2, R^{4a}$
is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 25 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2, R^{4a}$
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 30 a compound of Formula (50) wherein R^3 is 2-
ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is
OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R^3 is cyclobutyl-
amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is
 $N(Me)CH_2CH=CH_2, R^{4a}$ is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R^3 is
 $N(Et)CH_2CH=CH_2, R^{4a}$ is Me, R^{4b} is H, R^{4c} is OMe,

- R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 15 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
 R^{4e} is H;
- 20 a compound of Formula (50) wherein R^3 is $N(Me)Et$, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R^3 is $N(Me)Bu$, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R^3 is
 $N(Me)$ propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R^3 is
 $NH(CH(CH_3)CH(CH_3)CH_3$, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R^3 is
 $N(CH_2CH_2OMe)Me$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is OMe and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is
N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
NH(CH(CH₃)CH₂CH₃), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and
R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H; and
- 30 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H.

2. A compound of Formula (60)



FORMULA (60)

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and
 5 pharmaceutically acceptable salt forms thereof, selected from the group:

a compound of Formula (60) wherein R³ is NHCH(ET)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

10

a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
 20

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is
N(Et)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
yl;

25 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-

methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

5

a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

10

a compound of Formula (60) wherein R³ is N(Me)cPr, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

15

a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

25

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
yl;

30

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-dimethylamino-4-methylpyrid-3-yl.

30 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 6-methoxy-4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is cyclobutyl-

- amino, Ar is 6- methoxy -4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 6- methoxy -4-methylpyrid-3-
yl;
- a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6- methoxy -4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
20 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 6- methoxy -4-methylpyrid-3-
yl;
- 25 a compound of Formula (60) wherein R³ is
N(Et)propargyl, Ar is 6- methoxy -4-methylpyrid-3-
yl;
- 30 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 6- methoxy -4-
methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, Ar is 6-methoxy -4-methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 6-methoxy -4-methylpyrid-3-
yl;

10 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 6-methoxy -4-methylpyrid-3-
yl;

15 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 6-methoxy -4-methylpyrid-3-
yl;

15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 6-methoxy -4-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH₂CH₃, Ar is 6-methoxy -4-methylpyrid-
3-yl;

25 a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-methoxy -4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-methoxy -4-methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar
is 6-methoxy -4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is

- 6 - methoxy -4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
30 N(Me)propargyl, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is

NHCH(CH₃)CH(CH₃)CH₃, Ar is 4-methoxy-6-methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;

10

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 4-methoxy-6-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is

N(CH₂CH₂OMe)Et, Ar is 4-methoxy-6-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;

25

a compound of Formula (60) wherein R³ is NH(CH(CH₃)CH₂CH₃), Ar is 4-methoxy-6-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 4-methoxy-6-methylpyrid-3-yl;

30

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂, Ar is 4-methoxy-6-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar

- is 6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 4,6-dimethylpyrid-3-yl;
- 20 20 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et Ar is
4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
4,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

N(Et)propargyl, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

5 NHCH(CH₃)CH(CH₃)CH₃, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-

CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is

N(CH₂CH₂OMe)Me, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

15 N(CH₂CH₂OMe)Et, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

N(CH₂CH₂OMe)Pr, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-

20 CH₂cPr, Ar is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

NHCH(CH₃)CH₂CH₃, Ar is 4,6-dimethylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar

is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,

Ar is 4,6-dimethylpyrid-3-yl;

30

a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar

is 4,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
4,6-dimethylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is 2-
ethylpiperid-1-yl, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 2,6-dimethylpyrid-3-yl;

10

a compound of Formula (60) wherein R³ is
N(Me)CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;

15

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr,
Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 2,6-dimethylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
2,6-dimethylpyrid-3-yl;

25

a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
2,6-dimethylpyrid-3-yl;

30

a compound of Formula (60) wherein R³ is
N(Me)propargyl, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is

NH(CH₂CH₃)CH(CH₃)CH₃, Ar is 2,6-dimethylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Me, Ar is 2,6-dimethylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Et, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
N(CH₂CH₂OMe)Pr, Ar is 2,6-dimethylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 2,6-dimethylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is NH(CH₂CH₃)CH₂CH₃, Ar is 2,6-dimethyl pyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 2,6-dimethyl pyrid-3-yl;

25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂, Ar is 2,6-dimethylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 2,6-dimethyl-pyrid-3-yl; and

30 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is 2,6-dimethyl-pyrid-3-yl.

3. A compound and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, wherein said compound is selected from the group:

4-((2-butyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

10 4-((2-butyl)amino)-2,7-dimethyl-8-(2,5-di methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

15 4-((3-pentyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

4-((3-pentyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

20 4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

25 4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

30 4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

35

4-(diallylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

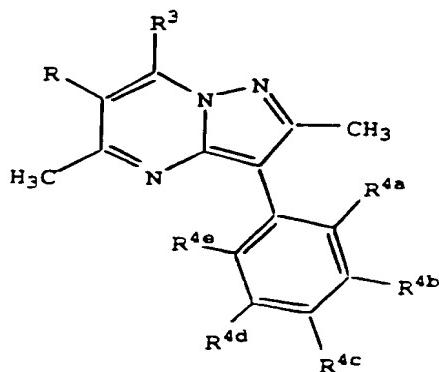
5 4-(diallylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine; and

10

4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine.

15 4. A compound of Formula (70)



20

FORMULA (70)

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof selected from the group:

a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

30

a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

5 a compound of Formula (70) wherein R is Cl, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (70) wherein R is Cl, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (70) wherein R is Cl, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (70) wherein R is Cl, R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (70) wherein R is Cl, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (70) wherein R is Cl, R³ is - NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

45 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is

- H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is - NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (70) wherein R is Cl, R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is (S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 10 a compound of Formula (70) wherein R is Cl, R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 15 a compound of Formula (70) wherein R is Cl, R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 20 a compound of Formula (70) wherein R is Cl, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 25 a compound of Formula (70) wherein R is Cl; R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 30 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 35 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 45 40 a compound of Formula (70) wherein R is Cl, R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 50 45 a compound of Formula (70) wherein R is Cl, R³ is -

- N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is -
NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is -
N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H
and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is -
N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is -
NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 25 20 a compound of Formula (70) wherein R is Cl, R³ is -
N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d}
is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is -
N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl,
R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is -
N(Bu)(Et), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is
H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is -
NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl,
R^{4d} is H and R^{4e} is H;

- H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is - NEt₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H; and
- 20 a compound of Formula (70) wherein R is Cl, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is Me, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is -N(n-Bu)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is Me, R³ is -

- N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is (S) - NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is (S) - NH(CH₂CH₂OMe)CH₂CMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H

and R^{4e} is H;

a compound of Formula (70) wherein R is Me, R^3 is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
5 R^{4d} is H and R^{4e} is H;

a compound of Formula (70) wherein R is Me, R^3 is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d}
10 is H and R^{4e} is H;

10 a compound of Formula (70) wherein R is Me, R^3 is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;

15 a compound of Formula (70) wherein R is Me, R^3 is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;

20 a compound of Formula (70) wherein R is Me, R^3 is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;

25 a compound of Formula (70) wherein R is Me, R^3 is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is H;

30 a compound of Formula (70) wherein R is Me, R^3 is -N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;

35 a compound of Formula (70) wherein R is Me, R^3 is -NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;

40 a compound of Formula (70) wherein R is Me, R^3 is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H
and R^{4e} is H;

a compound of Formula (70) wherein R is Me, R^3 is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;

- a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is - a compound of Formula (70) wherein R is Me, R³ is -

NET₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H; and

5 a compound of Formula (70) wherein R is Me, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (70) wherein R is F, R³ is - NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (70) wherein R is F, R³ is - N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (70) wherein R is F, R³ is - NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (70) wherein R is F, R³ is - N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is -N(n-Bu)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is -(S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -NH(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is -NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is F, R³ is (S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is (S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -NHCH(n-Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -NHCH

- (n-Pr) (CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me,
R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R³ is -
NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is -
NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is -
N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is -
NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is -
N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is -
NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
OMe and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is -
N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d}
is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -
N(Pr) (CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl,

R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (70) wherein R is F, R³ is - N(Bu)(Et), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is -NET₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H; and
- 35 a compound of Formula (70) wherein R is F, R³ is - N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (70) wherein R is Cl, R³ is -
N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is -
NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is -
NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is -
NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Cl, R³ is -NH-
2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Cl, R³ is
cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Cl, R³ is -
N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Cl, R³ is -
N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Cl, R³ is -
NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;

- a compound of Formula (70) wherein R is Cl, R³ is - NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Cl, R³ is - NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Cl, R³ is -NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Cl, R³ is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is F, R³ is - N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R³ is - N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R³ is - N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R³ is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R³ is -NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is -NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R³ is -NH-2-

- butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is F, R^3 is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is F, R^3 is - $N(Pr)(CH_2CH_2OMe)$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is F, R^3 is - $N(Et)(CH_2CH_2OMe)$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 15 a compound of Formula (70) wherein R is F, R^3 is - $N(Me)(CH_2CH_2OMe)$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is F, R^3 is - NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is F, R^3 is - NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is F, R^3 is - $NMeBu$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is F, R^3 is - NH-2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is F, R^3 is cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is Me, R^3 is -

- N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (70) wherein R is Me, R³ is -
 N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (70) wherein R is Me, R³ is -
 N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (70) wherein R is Me, R³ is -
 NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 20 a compound of Formula (70) wherein R is Me, R³ is -
 NMMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 25 a compound of Formula (70) wherein R is Me, R³ is -NH-
 2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 30 a compound of Formula (70) wherein R is Me, R³ is
 cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (70) wherein R is Me, R³ is -
 N(Pr)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (70) wherein R is Me, R³ is -
 N(Et)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- a compound of Formula (70) wherein R is Me, R³ is -

N(Me)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H;

5 a compound of Formula (70) wherein R is Me, R³ is -
NMeEt, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;

10 a compound of Formula (70) wherein R is Me, R³ is -
NMePr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;

15 a compound of Formula (70) wherein R is Me, R³ is -
NMeBu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;

20 a compound of Formula (70) wherein R is Me, R³ is -NH-
2-butyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
Me and R^{4e} is H; and

25 a compound of Formula (70) wherein R is Me, R³ is
cyclobutylamino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is Me and R^{4e} is H.

5. A compound and isomers thereof, stereoisomeric
25 forms thereof, or mixtures of stereoisomeric forms
thereof, and pharmaceutically acceptable salt forms
thereof, wherein said compound is selected from: 7-
(diethylamino)-2,5-dimethyl-3-(2-methyl-4-
methoxyphenyl-[1,5-a]-pyrazolopyrimidine and 7-(N-
30 (3-cyanopropyl)-N-propylamino)-2,5-dimethyl-3-(2,4-
dimethylphenyl)-[1,5-a]-pyrazolopyrimidine.

6. A pharmaceutical composition comprising a
pharmaceutically acceptable carrier and a
35 therapeutically effective amount of a compound of
claims 1, 2, 3, 4 and 5.

7. A method of treating affective disorder, anxiety,

depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder,
5 drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy,
10 stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals comprising administering
15 to the mammal a therapeutically effective amount of a compound of claims 1, 2, 3, 4 and 5.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/01824

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 C07D487/04 A61K31/495 // (C07D487/04, 251:00, 231:00),
 (C07D487/04, 239:00, 231:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	WO 98 03510 A (DU PONT MERCK PHARMA) 29 January 1998 see compounds 358, 378, page 119; 569, page 142; page 49, lines 14,24,28 and 31 ----	1
Y	WO 97 29109 A (JANSSEN PHARMACEUTICA NV ;NEUROCRINE BIOSCIENCES INC (US); CHEN CH) 14 August 1997 see abstract; claims ----	1-7
Y	WO 95 33750 A (PFIZER ;CHEN YUH PYNG L (US)) 14 December 1995 see abstract; claims ----	1-7
Y	WO 96 35689 A (NEUROGEN CORP ;YUAN JUN (US); HUTCHISON ALAN (US)) 14 November 1996 see abstract; claims -----	1-7

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

30 June 1999

06/07/1999

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/01824

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 7
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim 7
is directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out. Specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l. Application No.

PCT/US 99/01824

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9803510 A	29-01-1998	AU 3894297 A EP 0915880 A HR 970413 A NO 990264 A		10-02-1998 19-05-1999 31-10-1998 10-03-1999
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